Prescription Fulfillment With the Specialty Pharmacy Network for SAMSCA® (tolvaptan)

SAMSCA is available to patients continuing treatment when leaving the hospital, through a network of select specialty pharmacies.

When preparing to discharge a patient with a SAMSCA prescription, please select a Network Pharmacy from the national list below, or from the list of local pharmacies on the following pages.

Before your patients leave the hospital, you can e-prescribe, phone-in or fax their prescriptions directly to a Network Pharmacy.

Plan ahead to help your patients fill their prescriptions upon discharge

Participating Pharmacies

Specialty Mail Order Pharmacies			
Accredo	www.accredo.com	Phone: 855-891-7977 Fax: 877-251-9381	8:00 AM-11:00 PM ET M-F; 8:00 AM-5:00 PM ET Sat Order cut-off time: 12 noon ET
Albertsons Companies Specialty Retail	http://albertsons.com/specialtycare	Phone: 877-466-8028 Fax: 877-466-8040	9:00 AM-9:00 PM ET M-F Order cut-off time: 3:00 PM ET
BriovaRx	www.briovarx.com	Phone: 855-427-4682 Fax: 877-342-4596	8:00 AM-10:00 PM ET M-F; 9:00 AM-8:00 PM ET Sat-Sun Order cut-off time: 5:00 PM ET
Cigna Specialty Pharmacy	www.cigna.com/specialty-pharmacy-services	Phone: 800-351-3606 Fax: 800-351-3616	24 hours, 7 days-a-week Order cut-off time: 4:00 PM ET
CVS Specialty Pharmacy	www.cvsspecialty.com	Phone: 800-237-2767 Fax: 800-323-2445	7:30 AM-9:00 PM ET M-F Order cut-off time: 5:00 PM ET M-F
DirectRx*	www.directrx.com	Phone: 877-497-6620 Fax: 877-892-4007	8:00 AM-7:00 PM ET M-F; 9:00 AM-3:00 PM ET Sat Order cut-off time: 7:00 PM ET M-F; 3:00 PM ET Sat
Premier Pharmacy Services	www.premierpharmacyservices.com	Phone 1: 800-540-4700 Phone 2: 714-865-5875 Fax: 800-975-2344	24 hours, 7 days-a-week Order cut-off time: 7:00 PM ET, Mon-Sat
Walgreens Specialty Pharmacy	www.walgreens.com/pharmacy/specialtypharmacy.jsp	Phone: 888-380-6187, option 2 Fax: 877-848-2793	24 hours, 7 days-a-week Order cut-off time: 4:00 PM ET
15Rx† ***Texas only***	www.15rx.com	Phone: 210-684-1579 Fax: 210-684-1581	9:30 AM-7:00 PM ET M-F; 10:00 AM-4:00 PM ET Sat Order cut-off time: 7:00 PM ET M-F; 4:00 PM ET Sat
Specialty Retail Pharmacies			
Albertsons Companies Specialty Care Safeway Pharmacy	http://albertsons.com/specialtycare All pharmacies at Acme, Albertsons, Albertsons Market, Amigos, Carrs, Jewel Osco, Market Street, Pavilions, Randalls, Safeway, Shaws, Star Market, Tom Thumb, and Vons locations.	Phone: 877-466-8028 Fax: 877-466-8040	8:00 AM-9:00 PM local time, 7 days-a-week Order cut-off time for next-day pick-up: 1:00 PM local time
15Rx Pharmacy #1 *Texas only*	10415 State Hwy 151, Suite 105 San Antonio, TX 78251	Phone: 210-684-1579 Fax: 210-684-1581	9:30 AM-7:00 PM ET M-F; 10:00 AM-4:00 PM ET Sat; Closed Sun
15Rx Pharmacy #2 *Texas only*	11212 State Hwy 151, Medical Plaza-2, Suite 110, San Antonio, TX 78251	Phone: 210-543-1579 Fax: 210-543-1581	9:30 AM-7:00 PM ET M-F; 10:00 AM-4:00 PM ET Sat; Closed Sun

Disclaimers and Limitations

*DirectRx is not licensed in the following states: AK, AR, KS, LA, NV, NM, OR, TN, VA

†15Rx is licensed in the following state: TX

Please see FULL PRESCRIBING INFORMATION, including **BOXED WARNING**, at end of this document.

Participating Pharmacies

Health System Pharmacies			
Walgreens at Diagnostic Medical Center	1700 Spring Hill Ave Mobile, AL 36604	Phone: 251-694-6059 Fax: 251-694-6851	8:30 AM-5:00 PM M-F; Closed Sat-Sun
Walgreens at Grandview Physician Plaza	3686 Grandview Pkwy, Suite 120 Birmingham, AL 35243	Phone: 205-595-0419 Fax: 205-591-9541	9:00 AM-5:00 PM M-F; Closed Sat-Sun
Walgreens at DCH Hospital Medical Towers	701 University Blvd E Tuscaloosa, AL 35401	Phone: 205-750-0041 Fax: 205-750-0361	9:00 AM-5:30 PM M-Th; 9:00 AM-3:00 PM Fri; Closed Sat-Sun
Walgreens at Jackson Hospital	1758 Park Place, Suite 102 Montgomery, AL 36106	Phone: 334-240-1537 Fax: 334-240-2449	8:00 AM-6:00 PM M-F; Closed Sat-Sun
Walgreens at Maude L Whatley Health Center	2731 Martin Luther King Jr Blvd Tuscaloosa, AL 35401	Phone: 205-345-1197 Fax: 205-345-1570	8:30 AM-5:30 PM M-Th; 8:30 AM-5:00 PM Fri; Closed Sat-Sun
Walgreens at St Vincent's Professional Office Building	500 S University Little Rock, AR 72205	Phone: 501-664-4121 Fax: 501-661-9831	8:00 AM-6:00 PM M-F; 8:00 AM-1:00 PM Sat; Closed Sun
Walgreens at Banner Desert Hospital	1432 S Dobson Rd, Suite 101 Mesa, AZ 85202	Phone: 480-461-0490 Fax: 480-461-6056	8:00 AM-5:00 PM M-F; Closed Sat-Sun
Walgreens at Desert Aids Project	1695 N Sunrise Way Palm Springs, CA 92262	Phone: 760-325-9370 Fax: 760-325-9374	8:00 AM-6:30 PM M-F; 9:00 AM-3:00 PM Sat; Closed Sun
Walgreens at Eisenhower Medical Center	39000 Bob Hope Dr Rancho Mirage, CA 92270	Phone: 760-773-1219 Fax: 760-773-4289	7:30 AM-5:30 PM M-F; Closed Sat-Sun
Community, a Walgreens Pharmacy	1399 Roxbury Dr Los Angeles, CA 90035	Phone: 310-203-1007 Fax: 310-552-5330	8:00 AM-6:00 PM M-F; 9:00 AM-1:00 PM Sat; Closed Sun
Walgreens Specialty Pharmacy	1020 29th St Sacramento, CA 95816	Phone: 916-738-3300	8:30 AM-5:30 PM M-F; 8:00 AM-Noon Sat; Closed Sun
Pioneer, a Walgreens Pharmacy	10990 Warner Ave, Suite A Fountain Valley, CA 92708	Phone: 714-962-7200 Fax: 714-965-0469	9:00 AM-6:00 PM M-F; 10:00 AM-2:00 PM Sat; Closed Sun
Community Center, a Walgreens Pharmacy - San Diego	640 University Ave San Diego, CA 92103	Phone: 619-295-6688 Fax: 619-294-3388	8:00 AM-6:00 PM M-F; 10:00 AM-2:00 PM Sat; Closed Sun
Walgreens at UCSF Medical Center at Parnassus	500 Parnassus, J Level: Room MU-145 San Francisco, CA 94143	Phone: 415-681-3394 Fax: 415-681-3984	8:30 AM-8:30 PM M-F; 9:00 AM-5:00 PM Sat-Sun
Walgreens at CPMC-St Lukes	1580 Valencia St San Francisco, CA 94110	Phone: 415-970-8001 Fax: 415-970-8005	9:00 AM-6:00 PM M-F; Closed Sat-Sun
Walgreens at Swedish Medical Center	499 E Hampden Ave, Suite 150 Englewood, CO 80113	Phone: 303-524-3750 Fax: 303-524-3767	8:00 AM-6:00 PM M-F; Closed Sat-Sun
Walgreens at Presbyterian/ St Luke's Medical Center	1601 E 19th Ave, Suite 4650, 4th Fl Denver, CO 80218	Phone: 303-656-4656 Fax: 303-656-4661	8:00 AM-6:00 PM M-F; Closed Sat-Sun
Walgreens at Smilow Cancer Center	53 Park St New Haven, CT 06511	Phone: 203-777-7809 Fax: 203-777-7829	8:00 AM-7:00 PM M-F; 9:00 AM-5:00 PM Sat; 9:00 AM-1:00 PM Sun
Walgreens at Yale on Chapel Street	1415 Chapel St New Haven, CT 06511	Phone: 203-777-7880 Fax: 203-777-7896	9:00 AM-5:00 PM M-F; 9:00 AM-Noon Sat; Closed Sun
Community, a Walgreens Pharmacy	1325 14th St NW Washington, DC 20005	Phone: 202-332-8811 Fax: 202-332-3880	9:00 AM-6:00 PM M-F; Closed Sat-Sun
Walgreens Pharmacy at Eden Hill Medical Center	200 Banning St, Suite 100 Dover, DE 19904	Phone: 302-734-9303 Fax: 302-734-9308	8:30 AM-5:00 PM M-F; Closed Sat-Sun
Walgreens at Sacred Heart Hospital	5149 N 9th Ave, Suite 1137 Pensacola, FL 32504	Phone: 850-477-7568 Fax: 850-477-6788	8:00 AM-6:00 PM M-F; Closed Sat-Sun
Walgreens Pharmacy at Palmetto Medical Plaza	7100 W 20th, Suite G177 Hialeah, FL 33016	Phone: 305-824-0696 Fax: 305-824-1075	8:00 AM-6:00 PM M-F; Closed Sat-Sun
Community, a Walgreens Pharmacy	2100 N Orange Ave, Suite B Orlando, FL 32804	Phone: 407-897-5292 Fax: 407-897-6635	9:00 AM-6:00 PM M-F; Closed Sat-Sun
Walgreens at Orlando Regional Medical Center	1200 Kuhl Ave Orlando, FL 32806	Phone: 407-849-5088 Fax: 407-849-3094	8:00 AM-6:00 PM M-F; Closed Sat-Sun
Walgreens at West Florida Hospital	8333 N Davis Hwy Pensacola, FL 32514	Phone: 850-494-2432 Fax: 850-494-2437	8:30 AM-6:00 PM M-F; Closed Sat-Sun

Please see FULL PRESCRIBING INFORMATION, including **BOXED WARNING**, at end of this document.

Participating Pharmacies

Health System Pharmacies (cont'd)			
Walgreens at Waterview Tower	1515 N Flagler Ave West Palm Beach, FL 33401	Phone: 561-366-1393 Fax: 561-366-4856	8:30 AM-6:00 PM M-F; Closed Sat-Sun
Walgreens at Gardens Medical Pavilion	3401 PGA Blvd, Suite 110 Palm Beach Gardens, FL 33410	Phone: 561-493-8840 Fax: 561-493-8847	8:30 AM-6:00 PM M-F; 8:30 AM-Noon Sat; Closed Sun
Walgreens at Sarasota Memorial Hospital	1921 Waldemere St, Suite 201 Sarasota, FL 34239	Phone: 941-955-6012 Fax: 941-955-6109	9:00 AM-5:30 PM M-F; Closed Sat-Sun
Community, a Walgreens Pharmacy	3030 1st Ave N St Petersburg, FL 33713	Phone: 727-322-5200 Fax: 727-322-5288	9:00 AM-5:30 PM M-F; Closed Sat-Sun
Walgreens at Largo Diagnostic Clinic	1301 Second Ave SW Largo, FL 33770	Phone: 727-581-9382 Fax: 727-585-5818	8:00 AM-5:00 PM M-F; Closed Sat-Sun
Walgreens at DeKalb Medical Center	2675 N Decatur Rd Decatur, GA 30033	Phone: 404-299-5411 Fax: 404-299-8370	8:30 AM-5:30 PM M-F; Closed Sat-Sun
Walgreens at Atlanta Medical Center	340 Boulevard NE, Suite 143 Atlanta, GA 30312	Phone: 404-525-8256 Fax: 404-525-8261	8:30 AM-5:30 PM M-F; Closed Sat-Sun
Walgreens at Piedmont Hospital	35 Collier Rd NW, Suite 100 Atlanta, GA 30309	Phone: 404-350-9772 Fax: 404-350-9865	8:00 AM-6:00 PM M-F; Closed Sat-Sun
Walgreens at Advocate Lutheran General Hospital	1775 W Dempster, Suite T01116 Park Ridge, IL 60068	Phone: 847-692-2184 Fax: 847-692-2407	9:00 AM-6:00 PM M-F; Closed Sat-Sun
Walgreens at ACCESS Community Health Center - Des Plaines	1 N Broadway St Des Plaines, IL 60016	Phone: 847-827-7556 Fax: 847-827-8263	8:30 AM-6:30 PM M-F; 9:00 AM-Noon Sat; Closed Sun
Walgreens at Rush Copley Medical Center	2040 Ogden Ave, #117 Aurora, IL 60504	Phone: 630-499-4392 Fax: 630-499-5340	9:00 AM-7:00 PM M-F; Closed Sat-Sun
Walgreens at Provena St Joseph Medical Center	301 Madison St Joliet, IL 60435	Phone: 815-744-4173 Fax: 815-744-6057	9:00 AM-6:00 PM M-F; Closed Sat-Sun
Walgreens at Northwestern Memorial Hospital	201 E Huron St, Suite 1-210 Chicago, IL 60611	Phone: 312-951-1084 Fax: 312-951-1227	7:00 AM-8:00 PM M-F; 8:00 AM-4:00 PM Sat-Sun
Walgreens at Advocate Christ Medical Center	4440 W 95th St Oak Lawn, IL 60453	Phone: 708-857-1935 Fax: 708-857-1987	8:00 AM-8:00 PM M-F; 10:00 AM-4:00 PM Sat; Closed Sun
Walgreens at MacNeal Hospital	3249 S Oak Park Ave, Suite T1201 Berwyn, IL 60402	Phone: 708-484-6693 Fax: 708-484-9205	9:00 AM-7:00 PM M-F; Closed Sat-Sun
Community, a Walgreens Pharmacy	912 W Belmont Ave Chicago, IL 60657	Phone: 773-665-8990 Fax: 773-665-9766	9:00 AM-6:30 PM M-F; Closed Sat-Sun
Walgreens at Aris Health by Howard Brown	3245 N Halsted St Chicago, IL 60657	Phone: 773-248-3160 Fax: 773-248-3203	9:00 AM-5:00 PM M&F; 10:00 AM-7:00 PM Tu; 9:00 AM-7:00 PM W&Th; Closed Sat-Sun
Walgreens at NMPG-Lakeview	1333 W Belmont Ave Chicago, IL 60657	Phone: 773-549-9485 Fax: 773-549-9626	8:00 AM-7:00 PM M-F; 9:00 AM-5:00 PM Sat-Sun
Walgreens at Northstar Health Care	2835 N Sheffield, Suite 505 Chicago, IL 60657	Phone: 773-348-3574 Fax: 773-348-4175	9:00 AM-7:00 PM M-Th; 9:00 AM-4:00 PM Fri; Closed Sat-Sun
Walgreens at Silver Cross Hospital	1890 Silver Cross Blvd, Suite 120 New Lenox, IL 60451	Phone: 815-485-2578 Fax: 815-485-2746	9:00 AM-7:00 PM M-Th; 9:00 AM-3:00 PM Fri; 9:00 AM-2:00 PM Sat; Closed Sun
Walgreens at Northwestern Memorial Hospital - Outpatient Care Pavilion	259 E Erie St, Suite 250 Chicago, IL 60611	Phone: 312-649-6707 Fax: 312-649-6796	10:00 AM-6:00 PM M-F; Closed Sat-Sun
Walgreens at Central Dupage Hospital	25 N Winfield Rd Winfield, IL 60190	Phone: 630-407-0340 Fax: 630-407-0338	9:00 AM-7:00 PM M-F; 9:00 AM-3:00 PM Sat; Closed Sun
Walgreens at Marion General Hospital	330 N Wabash Ave, Suite 100 Marion, IN 46952	Phone: 765-664-2247 Fax: 765-664-2328	8:30 AM-5:00 PM M-F; Closed Sat-Sun
Community, a Walgreens Pharmacy	9002 N Meridian St, Suite 213 Indianapolis, IN 46260	Phone: 317-587-7400 Fax: 317-587-7410	8:30 AM-5:00 PM M-F; Closed Sat-Sun
Walgreens at Lutheran Hospital	7950 W Jefferson Blvd, Suite 1B005 Fort Wayne, IN 46804	Phone: 260-432-3110 Fax: 260-432-2990	8:00 AM-5:00 PM M-F; Closed Sat-Sun
Walgreens at Slidell Memorial Hospital	1051 Gause Blvd, MOB1 Slidell, LA 70458	Phone: 985-645-9934 Fax: 985-645-9940	8:30 AM-5:00 PM M-F; Closed Sat-Sun

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Participating Pharmacies

Health System Pharmacies (cont'd)			
Walgreens at Tulane Medical Center	1415 Tulane Ave, Suite 2CW07 New Orleans, LA 70112	Phone: 504-525-4534 Fax: 504-525-7019	9:00 AM-6:00 PM M-F; Closed Sat-Sun
Walgreens at Greater New Bedford Community Health Center	874 Purchase St New Bedford, MA 02740	Phone: 508-992-3209 Fax: 508-992-3783	8:00 AM-8:00 PM M-F; 8:00 AM-4:30 PM Sat; 8:00 AM-2:30 PM Sun
Community, a Walgreens Pharmacy	6 N Howard St Baltimore, MD 21201	Phone: 410-951-5940 Fax: 410-951-5946	9:00 AM-5:30 PM M-F; Closed Sat-Sun
Walgreens at Robinwood Professional Center	11110 Medical Campus Rd Hagerstown, MD 21742	Phone: 301-791-5373 Fax: 301-791-2416	7:00 AM-7:00 PM M-F; 9:00 AM-4:00 PM Sat-Sun
Walgreens at Sylvania Building	13424 Pennsylvania Ave Hagerstown, MD 21742	Phone: 301-797-8038 Fax: 301-797-4202	9:00 AM-6:00 PM M-F; 9:00 AM-4:00 PM Sat; Closed Sun
Community, a Walgreens Pharmacy	2100 Lyndale Ave S, Suite A Minneapolis, MN 55405	Phone: 612-872-7808 Fax: 612-874-1084	8:30 AM-6:00 PM M-F; Closed Sat-Sun
Walgreens at St Louis University Medical Center	3660 Vista Ave, Suite 101 St Louis, MO 63110	Phone: 314-771-2900 Fax: 314-771-2955	9:00 AM-5:00 PM M-F; Closed Sat-Sun
Community, a Walgreens Pharmacy	115A N Euclid Ave St Louis, MO 63108	Phone: 314-454-6676 Fax: 314-367-1882	8:30 AM-6:00 PM M-F; Closed Sat-Sun
Community, a Walgreens Pharmacy at Duke University Hospital	2816 Erwin Rd Durham, NC 27705	Phone: 919-282-5553 Fax: 919-864-4900	9:00 AM-5:30 PM M-F; Closed Sat-Sun
Walgreens Specialty Pharmacy	240 S 77th St Omaha, NE 68114	Phone: 402-397-5906 Fax: 402-397-0211	8:30 AM-5:30 PM M-F; 8:00 AM-Noon Sat; Closed Sun
Walgreens at Robert Wood Johnson University Hospital	One Robert Wood Johnson Place New Brunswick, NJ 08903	Phone: 732-246-1745 Fax: 732-249-0967	8:00 AM-8:00 PM M-F; 9:00 AM-6:00 PM Sat; 10:00 AM-6:00 PM Sun
Health System Pharmacy	364 Springfield Ave Summit, NJ 07901	Phone: 908-277-2092 Fax: 908-277-2592	8:00 AM-7:00 PM M-F; 9:00 AM-5:00 PM Sat; Closed Sun
Walgreens at Our Lady of Lourdes Medical Center	1600 Haddon Ave Camden, NJ 08103	Phone: 856-757-9601 Fax: 856-757-0307	9:00 AM-5:30 PM M-F; Closed Sat-Sun
Walgreens at Virtua Health System	200 Bowman Dr, Suite E-140 Voorhees, NJ 08043	Phone: 856-768-1873 Fax: 856-768-0218	9:00 AM-5:30 PM M-F; Closed Sat-Sun
Community, a Walgreens Pharmacy	901 S Rancho Dr, Suite 20 Las Vegas, NV 89106	Phone: 702-471-7828 Fax: 702-471-7805	8:30 AM-5:30 PM M-F; Closed Sat-Sun
Walgreens at Mountain View Hospital	3150 N Tenaya Way, Suite 170 Las Vegas, NV 89128	Phone: 702-256-2059 Fax: 702-256-2079	8:30 AM-5:30 PM M-F; Closed Sat-Sun
Community, a Walgreens Pharmacy	2226 White Plains Rd Bronx, NY 10467	Phone: 718-547-0077 Fax: 718-547-0013	8:00 AM-7:00 PM M-F; 9:00 AM-5:00 PM Sat; Closed Sun
Walgreens at New York Presbyterian Hospital	525 E 68th St, Suite F New York, NY 10065	Phone: 212-249-6451 Fax: 212-249-7028	8:00 AM-10:00 PM Sun-Sat
Walgreens at St Rita's Medical Center	730 W Market St Lima, OH 45801	Phone: 419-221-0166 Fax: 419-221-2962	9:00 AM-5:00 PM M-F; Closed Sat-Sun
Walgreens at Smith Clinic	1040 Delaware Ave Marion, OH 43302	Phone: 740-383-4529 Fax: 740-383-4591	8:30 AM-8:00 PM M-F; 8:30 AM-3:00 PM Sat; Closed Sun
Walgreens at Ohio State University at Doan Hall	410 W 10th Ave, #111 Columbus, OH 43210	Phone: 614-294-2018 Fax: 614-294-3926	8:00 AM-9:00 PM M-F; 9:00 AM-6:00 PM Sat-Sun
Walgreens at Ohio State University - East Hospital	1492 E Broad St Columbus, OH 43205	Phone: 614-252-7538 Fax: 614-258-7271	9:00 AM-7:00 PM M-F; 9:00 AM-3:00 PM Sat-Sun
Walgreens at Oklahoma State University Medical Center	717 S Houston Ave, Suite 103 Tulsa, OK 74127	Phone: 918-585-1957 Fax: 918-585-5607	8:00 AM-6:00 PM M-F; Closed Sat-Sun
Walgreens at St Anthony Hospital	535 NW 9th St, Suite 103 Oklahoma City, OK 73102	Phone: 405-231-2133 Fax: 405-231-1719	8:00 AM-6:00 PM M-F; Closed Sat-Sun
Walgreens at Lankenau Hospital	100 E Lancaster Ave, Suite 12 Wynnewood, PA 19096	Phone: 610-658-8640 Fax: 610-658-8644	7:00 AM-7:00 PM M-F; 9:00 AM-1:00 PM Sat; Closed Sun
Community, a Walgreens Pharmacy	65 Infanteria Shopping Ctr, Suite 101 San Juan, PR 00925	Phone: 787-777-1120 Fax: 787-777-1545	8:00 AM-5:00 PM M-F; Closed Sat-Sun

Please see FULL PRESCRIBING INFORMATION, including **BOXED WARNING**, at end of this document.

Participating Pharmacies

Health System Pharmacies (cont'd)			
Walgreens Pharmacy at Providence Community Health Center	335 Prairie Ave Providence, RI 02905	Phone: 401-781-4325 Fax: 401-781-4392	8:00 AM-8:00 PM M-Th; 8:00 AM-6:00 PM Fri; 9:00 AM-5:00 PM Sat-Sun
Walgreens at St Francis Medical Center	6005 Park Ave, Suite 108 Memphis, TN 38119	Phone: 901-682-8021 Fax: 901-682-8312	8:30 AM-5:00 PM M-F; Closed Sat-Sun
Walgreens at Bristol Regional Medical Center	One Medical Park Blvd, Suite 106-E Bristol, TN 37620	Phone: 423-844-2888 Fax: 423-844-0539	7:00 AM-9:00 PM M-F; 10:00 AM-2:00 PM Sat; Closed Sun
Walgreens at Holston Valley Medical Center	130 West Ravine, Suite 101 Kingsport, TN 37660	Phone: 423-224-6860 Fax: 423-224-5654	7:00 AM-7:00 PM M-F; 9:00 AM-5:00 PM Sat; 10:00 AM-2:00 PM Sun
Community, a Walgreens Pharmacy	1424 Union Ave Memphis, TN 38104	Phone: 901-725-7828 Fax: 901-725-7920	8:30 AM-5:30 PM M-F; Closed Sat-Sun
Walgreens at Barlite Pharmacy	7333 Barlite Blvd San Antonio, TX 78224	Phone: 210-924-6471 Fax: 210-924-6473	8:30 AM-6:30 PM M-F; 9:00 AM-1:00 PM Sat; Closed Sun
Walgreens at Memorial Hermann Hospital	11914 Astoria Blvd, Suite 190 Houston, TX 77089	Phone: 281-481-2434 Fax: 713-795-0094	8:30 AM-6:00 PM M-F; Closed Sat-Sun
Walgreens Pharmacy at Methodist Sugarland Hospital	16605 Southwest Fwy MOB3, Suite 100 Sugar Land, TX 77479	Phone: 281-980-0293 Fax: 281-494-0417	8:30 AM-5:30 PM M-F; Closed Sat-Sun
Walgreens at Memorial Hermann SW Hospital	7777 Southwest Fwy, Suite 104 Houston, TX 77074	Phone: 713-270-0632 Fax: 713-270-5263	8:30 AM-6:00 PM M-F; Closed Sat-Sun
Walgreens at St Lukes Episcopal Hospital	6624 Fannin St, 120 Houston, TX 77030	Phone: 713-795-0199 Fax: 713-795-0318	8:30 AM-6:00 PM M-F; Closed Sat-Sun
Walgreens at Harris Methodist Fort Worth Hospital	1325 Pennsylvania Ave, Suite 60 Fort Worth, TX 76104	Phone: 817-882-8670 Fax: 817-882-8792	8:30 AM-6:00 PM M-F; Closed Sat-Sun
Walgreens at UT Southwestern	5959 Harry Hines Blvd, Suite 100 Dallas, TX 75235	Phone: 214-630-6252 Fax: 214-879-9999	8:30 AM-5:30 PM M-F; Closed Sat-Sun
Walgreens at Memorial Hermann Hospital-TMC	6400 Fannin St, Suite 102 Houston, TX 77030	Phone: 713-799-2459 Fax: 713-799-2892	8:30 AM-6:00 PM M-F; Closed Sat-Sun
Walgreens at Methodist Hospital - Scurlock Tower	6560 Fannin St, Suite 260 Houston, TX 77030	Phone: 713-797-1410 Fax: 713-797-1501	7:00 AM-6:00 PM M-F; Closed Sat-Sun
Walgreens at Womans Hospital of Texas	7400 Fannin St, Suite 120 Houston, TX 77030	Phone: 713-795-4111 Fax: 713-795-0094	9:00 AM-6:00 PM M-F; Closed Sat-Sun
Community, a Walgreens Pharmacy	312 E Broad St, Suite 101 Richmond, VA 23219	Phone: 804-655-4419 Fax: 804-655-4421	8:30 AM-5:00 PM M-F; Closed Sat-Sun
Community, a Walgreens Pharmacy	1409 11th Ave Seattle, WA 98122	Phone: 206-324-2335 Fax: 206-324-2274	8:30 AM-6:30 PM M-F; 10:00 AM-2:00 PM Sat; Closed Sun
Platters, a Walgreens Pharmacy	400 E 5th Ave, Suite 102 Spokane, WA 99202	Phone: 509-838-0175 Fax: 509-838-2660	8:00 AM-6:00 PM M-F; 9:00 AM-1:00 PM Sat; Closed Sun
Walgreens at St Michael's Hospital	900 Illinois Ave Stevens Point, WI 54481	Phone: 715-344-6834 Fax: 715-344-7102	9:00 AM-5:00 PM M-F; Closed Sat-Sun

Please see FULL PRESCRIBING INFORMATION, including **BOXED WARNING**, at end of this document.

Otsuka

Otsuka America Pharmaceutical, Inc.

June 2017 07US17EBP0084

SAMSCA® (tolvaptan)

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use SAMSCA safely and effectively. See full prescribing information for SAMSCA.

SAMSCA® (tolvaptan) tablets for oral use
Initial U.S. Approval: 2009

WARNING: INITIATE AND RE-INITIATE IN A HOSPITAL AND MONITOR SERUM SODIUM

See full prescribing information for complete boxed warning.

- **SAMSCA should be initiated and re-initiated in patients only in a hospital where serum sodium can be monitored closely.**
- **Too rapid correction of hyponatremia (e.g., >12 mEq/L/24 hours) can cause osmotic demyelination resulting in dysarthria, mutism, dysphagia, lethargy, affective changes, spastic quadriparesis, seizures, coma and death. In susceptible patients, including those with severe malnutrition, alcoholism or advanced liver disease, slower rates of correction may be advisable.**

----------RECENT MAJOR CHANGES----------

Warnings and Precautions
Too Rapid Correction of Serum Sodium Can Cause Serious Neurologic Sequelae (see BOXED WARNING) (5.1) 06/2017

----------INDICATIONS AND USAGE----------

SAMSCA is a selective vasopressin V_2-receptor antagonist indicated for the treatment of clinically significant hypervolemic and euvolemic hyponatremia [serum sodium <125 mEq/L or less marked hyponatremia that is symptomatic and has resisted correction with fluid restriction], including patients with heart failure and Syndrome of Inappropriate Antidiuretic Hormone (SIADH) (1)

Important Limitations:
- Patients requiring intervention to raise serum sodium urgently to prevent or to treat serious neurological symptoms should not be treated with SAMSCA (1)
- It has not been established that SAMSCA provides a symptomatic benefit to patients (1)

SAMSCA® (tolvaptan)

----------DOSAGE AND ADMINISTRATION----------

- SAMSCA should be initiated and re-initiated in a hospital (2.1)
- The recommended starting dose is 15 mg once daily. Dosage may be increased at intervals ≥24 hr to 30 mg once daily, and to a maximum of 60 mg once daily as needed to raise serum sodium. (2.1)

----------DOSAGE FORMS AND STRENGTHS----------

- Tablets: 15 mg and 30 mg (3)

----------CONTRAINDICATIONS----------

- Need to raise serum sodium acutely (4.1)
- Patients who are unable to respond appropriately to thirst (4.2)
- Hypovolemic hyponatremia (4.3)
- Concomitant use of strong CYP 3A inhibitors (4.4)
- Anuria (4.5)
- Hypersensitivity (4.6)

----------WARNINGS/PRECAUTIONS----------

- Liver injury: Limit treatment duration to 30 days. If hepatic injury is suspected, discontinue SAMSCA. Avoid use in patients with underlying liver disease (5.2)
- Dehydration and hypovolemia may require intervention (5.3)
- Avoid use with hypertonic saline (5.4)
- Avoid use with CYP 3A inducers and moderate CYP 3A inhibitors (5.5)
- Consider dose reduction if co-administered with P-gp inhibitors (5.5)
- Monitor serum potassium in patients with potassium >5 mEq/L or on drugs known to increase potassium (5.6)

----------ADVERSE REACTIONS----------

Most common adverse reactions (≥5% placebo) are thirst, dry mouth, asthenia, constipation, pollakiuria or polyuria, and hyperglycemia (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Otsuka at 1-877-726-7220 or FDA at 1-800-FDA-1088 (*www.fda.gov/medwatch*).

----------USE IN SPECIFIC POPULATIONS----------

- Pregnancy: Based on animal data, may cause fetal harm (8.1)
- Nursing mothers: Discontinue drug or nursing taking into consideration importance of drug to mother (8.3)
- Pediatric Use: There are no studies (8.4)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 06/2017

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

WARNING: INITIATE AND RE-INITIATE IN A HOSPITAL AND MONITOR SERUM SODIUM

SAMSCA should be initiated and re-initiated in patients only in a hospital where serum sodium can be monitored closely.

Too rapid correction of hyponatremia (e.g., >12 mEq/L/24 hours) can cause osmotic demyelination resulting in dysarthria, mutism, dysphagia, lethargy, affective changes, spastic quadriparesis, seizures, coma and death. In susceptible patients, including those with severe malnutrition, alcoholism or advanced liver disease, slower rates of correction may be advisable.

1 INDICATIONS AND USAGE

SAMSCA® is indicated for the treatment of clinically significant hypervolemic and euvolemic hyponatremia (serum sodium <125 mEq/L or less marked hyponatremia that is symptomatic and has resisted correction with fluid restriction), including patients with heart failure and Syndrome of Inappropriate Antidiuretic Hormone (SIADH).

Important Limitations

Patients requiring intervention to raise serum sodium urgently to prevent or to treat serious neurological symptoms should not be treated with SAMSCA.

It has not been established that raising serum sodium with SAMSCA provides a symptomatic benefit to patients.

2 DOSAGE AND ADMINISTRATION

2.1 Usual Dosage in Adults

Patients should be in a hospital for initiation and re-initiation of therapy to evaluate the therapeutic response and because too rapid correction of hyponatremia can cause osmotic demyelination resulting in dysarthria, mutism, dysphagia, lethargy, affective changes, spastic quadriparesis, seizures, coma and death.

The usual starting dose for SAMSCA is 15 mg administered once daily without regard to meals. Increase the dose to 30 mg once daily, after at least 24 hours, to a maximum of 60 mg once daily, as needed to achieve the desired level of serum sodium. Do not administer SAMSCA for more than 30 days to minimize the risk of liver injury *[see Warnings and Precautions (5.2)]*.

During initiation and titration, frequently monitor for changes in serum electrolytes and volume. Avoid fluid restriction during the first 24 hours of therapy. Patients receiving SAMSCA should be advised that they can continue ingestion of fluid in response to thirst *[see Warnings and Precautions (5.1)]*.

2.2 Drug Withdrawal

Following discontinuation from SAMSCA, patients should be advised to resume fluid restriction and should be monitored for changes in serum sodium and volume status.

2.3 Co-Administration with CYP 3A Inhibitors, CYP 3A Inducers and P-gp Inhibitors

CYP 3A Inhibitors

Tolvaptan is metabolized by CYP 3A, and use with strong CYP 3A inhibitors causes a marked (5-fold) increase in exposure *[see Contraindications (4.4)]*. The effect of moderate CYP 3A inhibitors on tolvaptan exposure has not been assessed. Avoid co-administration of SAMSCA and moderate CYP 3A inhibitors *[see Warnings and Precautions (5.5), Drug Interactions (7.1)]*.

CYP 3A Inducers

Co-administration of SAMSCA with potent CYP 3A inducers (e.g., rifampin) reduces tolvaptan plasma concentrations by 85%. Therefore, the expected clinical effects of SAMSCA may not be observed at the recommended dose. Patient response should be monitored and the dose adjusted accordingly *[see Warnings and Precautions (5.5), Drug Interactions (7.1)]*.

P-gp Inhibitors

Tolvaptan is a substrate of P-gp. Co-administration of SAMSCA with inhibitors of P-gp (e.g., cyclosporine) may necessitate a decrease in SAMSCA dose *[see Warnings and Precautions (5.5), Drug Interactions (7.1)]*.

3 DOSAGE FORMS AND STRENGTHS

SAMSCA (tolvaptan) is available in 15 mg and 30 mg tablets *[see How Supplied/Storage and Handling (16)]*.

4 CONTRAINDICATIONS

SAMSCA is contraindicated in the following conditions:

4.1 Urgent Need to Raise Serum Sodium Acutely

SAMSCA has not been studied in a setting of urgent need to raise serum sodium acutely.

4.2 Inability of the Patient to Sense or Appropriately Respond to Thirst

Patients who are unable to auto-regulate fluid balance are at substantially increased risk of incurring an overly rapid correction of serum sodium, hypernatremia and hypovolemia.

4.3 Hypovolemic Hyponatremia

Risks associated with worsening hypovolemia, including complications such as hypotension and renal failure, outweigh possible benefits.

4.4 Concomitant Use of Strong CYP 3A Inhibitors

Ketoconazole 200 mg administered with tolvaptan increased tolvaptan exposure by 5-fold. Larger doses would be expected to produce larger increases in tolvaptan exposure. There is not adequate experience to define the dose adjustment that would be needed to allow safe use of tolvaptan with strong CYP 3A inhibitors such as clarithromycin, ketoconazole, itraconazole, ritonavir, indinavir, nelfinavir, saquinavir, nefazodone, and telithromycin.

SAMSCA® (tolvaptan)

4.5 Anuric Patients

In patients unable to make urine, no clinical benefit can be expected.

4.6 Hypersensitivity

SAMSCA is contraindicated in patients with hypersensitivity (e.g. anaphylactic shock, rash generalized) to tolvaptan or any component of the product *[see Adverse Reactions (6.2)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Too Rapid Correction of Serum Sodium Can Cause Serious Neurologic Sequelae (see BOXED WARNING)

Osmotic demyelination syndrome is a risk associated with too rapid correction of hyponatremia (e.g., >12 mEq/L/24 hours). Osmotic demyelination results in dysarthria, mutism, dysphagia, lethargy, affective changes, spastic quadriparesis, seizures, coma or death. In susceptible patients, including those with severe malnutrition, alcoholism or advanced liver disease, slower rates of correction may be advisable. In controlled clinical trials in which tolvaptan was administered in titrated doses starting at 15 mg once daily, 7% of tolvaptan-treated subjects with a serum sodium <130 mEq/L had an increase in serum sodium greater than 8 mEq/L at approximately 8 hours and 2% had an increase greater than 12 mEq/L at 24 hours. Approximately 1% of placebo-treated subjects with a serum sodium <130 mEq/L had a rise greater than 8 mEq/L at 8 hours and no patient had a rise greater than 12 mEq/L/24 hours. Osmotic demyelination syndrome has been reported in association with SAMSCA therapy *[see Adverse Reactions (6.2)]*. Patients treated with SAMSCA should be monitored to assess serum sodium concentrations and neurologic status, especially during initiation and after titration. Subjects with SIADH or very low baseline serum sodium concentrations may be at greater risk for too-rapid correction of serum sodium. In patients receiving SAMSCA who develop too rapid a rise in serum sodium, discontinue or interrupt treatment with SAMSCA and consider administration of hypotonic fluid. Fluid restriction during the first 24 hours of therapy with SAMSCA may increase the likelihood of overly-rapid correction of serum sodium, and should generally be avoided. Co-administration of diuretics also increases the risk of too rapid correction of serum sodium and such patients should undergo close monitoring of serum sodium.

5.2 Liver Injury

SAMSCA can cause serious and potentially fatal liver injury. In a placebo-controlled and open label extension study of chronically administered tolvaptan in patients with autosomal dominant polycystic kidney disease, cases of serious liver injury attributed to tolvaptan were observed. An increased incidence of ALT greater than three times the upper limit of normal was associated with tolvaptan (42/958 or 4.4%) compared to placebo (5/484 or 1.0%). Cases of serious liver injury were generally observed starting 3 months after initiation of tolvaptan although elevations of ALT occurred prior to 3 months.

Patients with symptoms that may indicate liver injury, including fatigue, anorexia, right upper abdominal discomfort, dark urine or jaundice should discontinue treatment with SAMSCA.

Limit duration of therapy with SAMSCA to 30 days. Avoid use in patients with underlying liver disease, including cirrhosis, because the ability to recover from liver injury may be impaired *[see Adverse Reactions (6.1)]*.

5.3 Dehydration and Hypovolemia

SAMSCA therapy induces copious aquaresis, which is normally partially offset by fluid intake. Dehydration and hypovolemia can occur, especially in potentially volume-depleted patients receiving diuretics or those who are fluid restricted. In multiple-dose, placebo-controlled trials in which 607 hyponatremic patients were treated with tolvaptan, the incidence of dehydration was 3.3% for tolvaptan and 1.5% for placebo-treated patients. In patients receiving SAMSCA who develop medically significant signs or symptoms of hypovolemia, interrupt or discontinue SAMSCA therapy and provide supportive care with careful management of vital signs, fluid balance and electrolytes. Fluid restriction during therapy with SAMSCA may increase the risk of dehydration and hypovolemia. Patients receiving SAMSCA should continue ingestion of fluid in response to thirst.

5.4 Co-administration with Hypertonic Saline

Concomitant use with hypertonic saline is not recommended.

5.5 Drug Interactions

Other Drugs Affecting Exposure to Tolvaptan

CYP 3A Inhibitors

Tolvaptan is a substrate of CYP 3A. CYP 3A inhibitors can lead to a marked increase in tolvaptan concentrations *[see Dosage and Administration (2.3), Drug Interactions (7.1)]*. Do not use SAMSCA with strong inhibitors of CYP 3A *[see Contraindications (4.4)]* and avoid concomitant use with moderate CYP 3A inhibitors.

CYP 3A Inducers

Avoid co-administration of CYP 3A inducers (e.g., rifampin, rifabutin, rifapentin, barbiturates, phenytoin, carbamazepine, St. John's Wort) with SAMSCA, as this can lead to a reduction in the plasma concentration of tolvaptan and decreased effectiveness of SAMSCA treatment. If co-administered with CYP 3A inducers, the dose of SAMSCA may need to be increased *[see Dosage and Administration (2.3), Drug Interactions (7.1)]*.

P-gp Inhibitors

The dose of SAMSCA may have to be reduced when SAMSCA is co-administered with P-gp inhibitors, e.g., cyclosporine *[see Dosage and Administration (2.3), Drug Interactions (7.1)]*.

5.6 Hyperkalemia or Drugs that Increase Serum Potassium

Treatment with tolvaptan is associated with an acute reduction of the extracellular fluid volume which could result in increased serum potassium. Serum potassium levels should be monitored after initiation of tolvaptan treatment in patients with a serum potassium >5 mEq/L as well as those who are receiving drugs known to increase serum potassium levels.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reactions rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. The adverse event information from clinical trials does, however, provide a basis for identifying the adverse events that appear to be related to drug use and for approximating rates.

In multiple-dose, placebo-controlled trials, 607 hyponatremic patients (serum sodium <135 mEq/L) were treated with SAMSCA. The mean age of these patients was 62 years; 70% of patients were male and 82% were Caucasian. One hundred eighty nine (189) tolvaptan-treated patients had a serum sodium <130 mEq/L, and 52 patients had a serum sodium <125 mEq/L. Hyponatremia was attributed to cirrhosis in 17% of patients, heart failure in 68% and SIADH/other in 16%. Of these patients, 223 were treated with the recommended dose titration (15 mg titrated to 60 mg as needed to raise serum sodium).

Overall, over 4,000 patients have been treated with oral doses of tolvaptan in open-label or placebo-controlled clinical trials. Approximately 650 of these patients had hyponatremia; approximately 219 of these hyponatremic patients were treated with tolvaptan for 6 months or more.

The most common adverse reactions (incidence ≥5% more than placebo) seen in two 30-day, double-blind, placebo-controlled hyponatremia trials in which tolvaptan was administered in titrated doses (15 mg to 60 mg once daily) were thirst, dry mouth, asthenia, constipation, pollakiuria or polyuria and hyperglycemia. In these trials, 10% (23/223) of tolvaptan-treated patients discontinued treatment because of an adverse event, compared to 12% (26/220) of placebo-treated patients; no adverse reaction resulting in discontinuation of trial medication occurred at an incidence of >1% in tolvaptan-treated patients.

Table 1 lists the adverse reactions reported in tolvaptan-treated patients with hyponatremia (serum sodium <135 mEq/L) and at a rate at least 2% greater than placebo-treated patients in two 30-day, double-blind, placebo-controlled trials. In these studies, 223 patients were exposed to tolvaptan (starting dose 15 mg, titrated to 30 and 60 mg as needed to raise serum sodium). Adverse events resulting in death in these trials were 6% in tolvaptan-treated-patients and 6% in placebo-treated patients.

Table 1. Adverse Reactions (>2% more than placebo) in Tolvaptan-Treated Patients in Double-Blind, Placebo-Controlled Hyponatremia Trials

System Organ Class MedDRA Preferred Term	Tolvaptan 15 mg/day-60 mg/day (N = 223) n (%)	Placebo (N = 220) n (%)
Gastrointestinal Disorders		
Dry mouth	28 (13)	9 (4)
Constipation	16 (7)	4 (2)
General Disorders and Administration Site Conditions		
Thirst[a]	35 (16)	11 (5)
Asthenia	19 (9)	9 (4)
Pyrexia	9 (4)	2 (1)
Metabolism and Nutrition Disorders		
Hyperglycemia[b]	14 (6)	2 (1)
Anorexia[c]	8 (4)	2 (1)
Renal and Urinary Disorders		
Pollakiuria or polyuria[d]	25 (11)	7 (3)

The following terms are subsumed under the referenced ADR in Table 1:
[a] polydipsia; [b] diabetes mellitus; [c] decreased appetite; [d] urine output increased, micturition urgency, nocturia

In a subgroup of patients with hyponatremia (N = 475, serum sodium <135 mEq/L) enrolled in a double-blind, placebo-controlled trial (mean duration of treatment was 9 months) of patients with worsening heart failure, the following adverse reactions occurred in tolvaptan-treated patients at a rate at least 2% greater than placebo: mortality (42% tolvaptan, 38% placebo), nausea (21% tolvaptan, 16% placebo), thirst (12% tolvaptan, 2% placebo), dry mouth (7% tolvaptan, 2% placebo) and polyuria or pollakiuria (4% tolvaptan, 1% placebo).

Gastrointestinal bleeding in patients with cirrhosis

In patients with cirrhosis treated with tolvaptan in the hyponatremia trials, gastrointestinal bleeding was reported in 6 out of 63 (10%) tolvaptan-treated patients and 1 out of 57 (2%) placebo treated patients.

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The following adverse reactions occurred in <2% of hyponatremic patients treated with SAMSCA and at a rate greater than placebo in double-blind placebo-controlled trials (N = 607 tolvaptan; N = 518 placebo) or in <2% of patients in an uncontrolled trial of patients with hyponatremia (N = 111) and are not mentioned elsewhere in the label.

Blood and Lymphatic System Disorders: Disseminated intravascular coagulation

Cardiac Disorders: Intracardiac thrombus, ventricular fibrillation

Investigations: Prothrombin time prolonged

Gastrointestinal Disorders: Ischemic colitis

Metabolism and Nutrition Disorders: Diabetic ketoacidosis

Musculoskeletal and Connective Tissue Disorders: Rhabdomyolysis

Nervous System: Cerebrovascular accident

Renal and Urinary Disorders: Urethral hemorrhage

Reproductive System and Breast Disorders (female): Vaginal hemorrhage

Respiratory, Thoracic, and Mediastinal Disorders: Pulmonary embolism, respiratory failure

Vascular disorder: Deep vein thrombosis

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of SAMSCA. Because these reactions are reported voluntarily from a population of an unknown size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Neurologic: Osmotic demyelination syndrome

Investigations: Hypernatremia

Removal of excess free body water increases serum osmolality and serum sodium concentrations. All patients treated with tolvaptan, especially those whose serum sodium levels become normal, should continue to be monitored to ensure serum sodium remains within normal limits. If hypernatremia is observed, management may include dose decreases or interruption of tolvaptan treatment, combined with modification of free-water intake or infusion. During clinical trials of hyponatremic patients, hypernatremia was reported as an adverse event in 0.7% of patients receiving tolvaptan vs. 0.6% of patients receiving placebo; analysis of laboratory values demonstrated an incidence of hypernatremia of 1.7% in patients receiving tolvaptan vs. 0.8% in patients receiving placebo.

Immune System Disorders: Hypersensitivity reactions including anaphylactic shock and rash generalized *[see Contraindications (4.6)]*.

7 DRUG INTERACTIONS

7.1 Effects of Drugs on Tolvaptan

Ketoconazole and Other Strong CYP 3A Inhibitors

SAMSCA is metabolized primarily by CYP 3A. Ketoconazole is a strong inhibitor of CYP 3A and also an inhibitor of P-gp. Co-administration of SAMSCA and ketoconazole 200 mg daily results in a 5-fold increase in exposure to tolvaptan. Co-administration of SAMSCA with 400 mg ketoconazole daily or with other strong CYP 3A inhibitors (e.g., clarithromycin, itraconazole, telithromycin, saquinavir, nelfinavir, ritonavir and nefazodone) at the highest labeled dose would be expected to cause an even greater increase in tolvaptan exposure. Thus, SAMSCA and strong CYP 3A inhibitors should not be co-administered *[see Dosage and Administration (2.3) and Contraindications (4.4)]*.

Moderate CYP 3A Inhibitors

The impact of moderate CYP 3A inhibitors (e.g., erythromycin, fluconazole, aprepitant, diltiazem and verapamil) on the exposure to co-administered tolvaptan has not been assessed. A substantial increase in the exposure to tolvaptan would be expected when SAMSCA is co-administered with moderate CYP 3A inhibitors. Co-administration of SAMSCA with moderate CYP 3A inhibitors should therefore generally be avoided *[see Dosage and Administration (2.3) and Warnings and Precautions (5.5)]*.

Grapefruit Juice

Co-administration of grapefruit juice and SAMSCA results in a 1.8-fold increase in exposure to tolvaptan *[see Dose and Administration (2.3) and Warnings and Precautions (5.5)]*.

P-gp Inhibitors

Reduction in the dose of SAMSCA may be required in patients concomitantly treated with P-gp inhibitors, such as e.g., cyclosporine, based on clinical response *[see Dose and Administration (2.3) and Warnings and Precautions (5.5)]*.

Rifampin and Other CYP 3A Inducers

Rifampin is an inducer of CYP 3A and P-gp. Co-administration of rifampin and SAMSCA reduces exposure to tolvaptan by 85%. Therefore, the expected clinical effects of SAMSCA in the presence of rifampin and other inducers (e.g., rifabutin, rifapentin, barbiturates, phenytoin, carbamazepine and St. John's Wort) may not be observed at the usual dose levels of SAMSCA. The dose of SAMSCA may have to be increased *[Dosage and Administration (2.3) and Warnings and Precautions (5.5)]*.

Lovastatin, Digoxin, Furosemide, and Hydrochlorothiazide

Co-administration of lovastatin, digoxin, furosemide, and hydrochlorothiazide with SAMSCA has no clinically relevant impact on the exposure to tolvaptan.

7.2 Effects of Tolvaptan on Other Drugs

Digoxin

Digoxin is a P-gp substrate. Co-administration of SAMSCA with digoxin increased digoxin AUC by 20% and Cmax by 30%.

Warfarin, Amiodarone, Furosemide, and Hydrochlorothiazide
Co-administration of tolvaptan does not appear to alter the pharmacokinetics of warfarin, furosemide, hydrochlorothiazide, or amiodarone (or its active metabolite, desethylamiodarone) to a clinically significant degree.

Lovastatin
SAMSCA is a weak inhibitor of CYP 3A. Co-administration of lovastatin and SAMSCA increases the exposure to lovastatin and its active metabolite lovastatin-β hydroxyacid by factors of 1.4 and 1.3, respectively. This is not a clinically relevant change.

Pharmacodynamic Interactions
Tolvaptan produces a greater 24 hour urine volume/excretion rate than does furosemide or hydrochlorothiazide. Concomitant administration of tolvaptan with furosemide or hydrochlorothiazide results in a 24 hour urine volume/excretion rate that is similar to the rate after tolvaptan administration alone.

Although specific interaction studies were not performed, in clinical studies tolvaptan was used concomitantly with beta-blockers, angiotensin receptor blockers, angiotensin converting enzyme inhibitors and potassium sparing diuretics. Adverse reactions of hyperkalemia were approximately 1-2% higher when tolvaptan was administered with angiotensin receptor blockers, angiotensin converting enzyme inhibitors and potassium sparing diuretics compared to administration of these medications with placebo. Serum potassium levels should be monitored during concomitant drug therapy.

As a V_2-receptor antagonist, tolvaptan may interfere with the V_2-agonist activity of desmopressin (dDAVP). In a male subject with mild Von Willebrand (vW) disease, intravenous infusion of dDAVP 2 hours after administration of oral tolvaptan did not produce the expected increases in vW Factor Antigen or Factor VIII activity. It is not recommended to administer SAMSCA with a V_2-agonist.

8 USE IN SPECIFIC POPULATIONS
There is no need to adjust dose based on age, gender, race, or cardiac function *[see Clinical Pharmacology (12.3)]*.

8.1 Pregnancy
Pregnancy Category C.
There are no adequate and well controlled studies of SAMSCA use in pregnant women. In animal studies, cleft palate, brachymelia, microphthalmia, skeletal malformations, decreased fetal weight, delayed fetal ossification, and embryo-fetal death occurred. SAMSCA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

In embryo-fetal development studies, pregnant rats and rabbits received oral tolvaptan during organogenesis. Rats received 2 to 162 times the maximum recommended human dose (MRHD) of tolvaptan (on a body surface area basis). Reduced fetal weights and delayed fetal ossification occurred at 162 times the MRHD. Signs of maternal toxicity (reduction in body weight gain and food consumption) occurred at 16 and 162 times the MRHD. When pregnant rabbits received oral tolvaptan at 32 to 324 times the MRHD (on a body surface area basis), there were reductions in maternal body weight gain and food consumption at all doses, and increased abortions at the mid and high doses (about 97 and 324 times the MRHD). At 324 times the MRHD, there were increased rates of embryo-fetal death, fetal microphthalmia, open eyelids, cleft palate, brachymelia and skeletal malformations *[see Nonclinical Toxicology (13.3)]*.

8.2 Labor and Delivery
The effect of SAMSCA on labor and delivery in humans is unknown.

8.3 Nursing Mothers
It is not known whether SAMSCA is excreted into human milk. Tolvaptan is excreted into the milk of lactating rats. Because many drugs are excreted into human milk and because of the potential for serious adverse reactions in nursing infants from SAMSCA, a decision should be made to discontinue nursing or SAMSCA, taking into consideration the importance of SAMSCA to the mother.

8.4 Pediatric Use
Safety and effectiveness of SAMSCA in pediatric patients have not been established.

8.5 Geriatric Use
Of the total number of hyponatremic subjects treated with SAMSCA in clinical studies, 42% were 65 and over, while 19% were 75 and over. 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. Increasing age has no effect on tolvaptan plasma concentrations.

8.6 Use in Patients with Hepatic Impairment
Moderate and severe hepatic impairment do not affect exposure to tolvaptan to a clinically relevant extent. Avoid use of tolvaptan in patients with underlying liver disease.

8.7 Use in Patients with Renal Impairment
No dose adjustment is necessary based on renal function. There are no clinical trial data in patients with CrCl <10 mL/min, and, because drug effects on serum sodium levels are likely lost at very low levels of renal function, use in patients with a CrCl <10 mL/min is not recommended. No benefit can be expected in patients who are anuric *[see Contraindications (4.5) and Clinical Pharmacology (12.3)]*.

8.8 Use in Patients with Congestive Heart Failure
The exposure to tolvaptan in patients with congestive heart failure is not clinically relevantly increased. No dose adjustment is necessary.

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10 OVERDOSAGE
Single oral doses up to 480 mg and multiple doses up to 300 mg once daily for 5 days have been well tolerated in studies in healthy subjects. There is no specific antidote for tolvaptan intoxication. The signs and symptoms of an acute overdose can be anticipated to be those of excessive pharmacologic effect: a rise in serum sodium concentration, polyuria, thirst, and dehydration/hypovolemia.

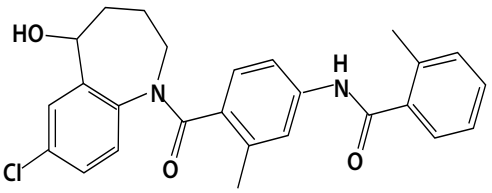
The oral LD_{50} of tolvaptan in rats and dogs is >2000 mg/kg. No mortality was observed in rats or dogs following single oral doses of 2000 mg/kg (maximum feasible dose). A single oral dose of 2000 mg/kg was lethal in mice, and symptoms of toxicity in affected mice included decreased locomotor activity, staggering gait, tremor and hypothermia.

If overdose occurs, estimation of the severity of poisoning is an important first step. A thorough history and details of overdose should be obtained, and a physical examination should be performed. The possibility of multiple drug involvement should be considered.

Treatment should involve symptomatic and supportive care, with respiratory, ECG and blood pressure monitoring and water/electrolyte supplements as needed. A profuse and prolonged aquaresis should be anticipated, which, if not matched by oral fluid ingestion, should be replaced with intravenous hypotonic fluids, while closely monitoring electrolytes and fluid balance.

ECG monitoring should begin immediately and continue until ECG parameters are within normal ranges. Dialysis may not be effective in removing tolvaptan because of its high binding affinity for human plasma protein (>99%). Close medical supervision and monitoring should continue until the patient recovers.

11 DESCRIPTION
Tolvaptan is (±)-4'-[(7-chloro-2,3,4,5-tetrahydro-5-hydroxy-1H-1-benzazepin-1-yl) carbonyl]-*o*-tolu-*m*-toluidide. The empirical formula is $C_{26}H_{25}ClN_2O_3$. Molecular weight is 448.94. The chemical structure is:



SAMSCA tablets for oral use contain 15 mg or 30 mg of tolvaptan. Inactive ingredients include corn starch, hydroxypropyl cellulose, lactose monohydrate, low-substituted hydroxypropyl cellulose, magnesium stearate and microcrystalline cellulose and FD&C Blue No. 2 Aluminum Lake as colorant.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action
Tolvaptan is a selective vasopressin V_2-receptor antagonist with an affinity for the V_2-receptor that is 1.8 times that of native arginine vasopressin (AVP). Tolvaptan affinity for the V_2-receptor is 29 times greater than for the V_{1a}-receptor. When taken orally, 15 to 60 mg doses of tolvaptan antagonize the effect of vasopressin and cause an increase in urine water excretion that results in an increase in free water clearance (aquaresis), a decrease in urine osmolality, and a resulting increase in serum sodium concentrations. Urinary excretion of sodium and potassium and plasma potassium concentrations are not significantly changed. Tolvaptan metabolites have no or weak antagonist activity for human V_2-receptors compared with tolvaptan.

Plasma concentrations of native AVP may increase (avg. 2-9 pg/mL) with tolvaptan administration.

12.2 Pharmacodynamics
In healthy subjects receiving a single dose of SAMSCA 60 mg, the onset of the aquaretic and sodium increasing effects occurs within 2 to 4 hours post-dose. A peak effect of about a 6 mEq increase in serum sodium and about 9 mL/min increase in urine excretion rate is observed between 4 and 8 hours post-dose; thus, the pharmacological activity lags behind the plasma concentrations of tolvaptan. About 60% of the peak effect on serum sodium is sustained at 24 hours post-dose, but the urinary excretion rate is no longer elevated by this time. Doses above 60 mg tolvaptan do not increase aquaresis or serum sodium further. The effects of tolvaptan in the recommended dose range of 15 to 60 mg once daily appear to be limited to aquaresis and the resulting increase in sodium concentration.

In a parallel-arm, double-blind (for tolvaptan and placebo), placebo- and positive-controlled, multiple dose study of the effect of tolvaptan on the QTc interval, 172 healthy subjects were randomized to tolvaptan 30 mg, tolvaptan 300 mg, placebo, or moxifloxacin 400 mg once daily. At both the 30 mg and 300 mg doses, no significant effect of administering tolvaptan on the QTc interval was detected on Day 1 and Day 5. At the 300 mg dose, peak tolvaptan plasma concentrations were approximately 4-fold higher than the peak concentrations following a 30 mg dose. Moxifloxacin increased the QT interval by 12 ms at 2 hours after dosing on Day 1 and 17 ms at 1 hour after dosing on Day 5, indicating that the study was adequately designed and conducted to detect tolvaptan's effect on the QT interval, had an effect been present.

12.3 Pharmacokinetics
In healthy subjects the pharmacokinetics of tolvaptan after single doses of up to 480 mg and multiple doses up to 300 mg once daily have been examined. Area under the curve (AUC) increases proportionally with dose. After administration of doses ≥60 mg, however, Cmax increases less than proportionally with dose. The pharmacokinetic properties of tolvaptan are stereospecific, with a steady-state ratio of the S-(-) to the R-(+) enantiomer of about 3. The absolute bioavailability of tolvaptan is unknown. At least 40% of the dose is absorbed

as tolvaptan or metabolites. Peak concentrations of tolvaptan are observed between 2 and 4 hours post-dose. Food does not impact the bioavailability of tolvaptan. *In vitro* data indicate that tolvaptan is a substrate and inhibitor of P-gp. Tolvaptan is highly plasma protein bound (99%) and distributed into an apparent volume of distribution of about 3 L/kg. Tolvaptan is eliminated entirely by non-renal routes and mainly, if not exclusively, metabolized by CYP 3A. After oral dosing, clearance is about 4 mL/min/kg and the terminal phase half-life is about 12 hours. The accumulation factor of tolvaptan with the once-daily regimen is 1.3 and the trough concentrations amount to ≤16% of the peak concentrations, suggesting a dominant half-life somewhat shorter than 12 hours. There is marked inter-subject variation in peak and average exposure to tolvaptan with a percent coefficient of variation ranging between 30 and 60%.

In patients with hyponatremia of any origin the clearance of tolvaptan is reduced to about 2 mL/min/kg. Moderate or severe hepatic impairment or congestive heart failure decrease the clearance and increase the volume of distribution of tolvaptan, but the respective changes are not clinically relevant. Exposure and response to tolvaptan in subjects with creatinine clearance ranging between 79 and 10 mL/min and patients with normal renal function are not different.

In a study in patients with creatinine clearances ranging from 10-124 mL/min administered a single dose of 60 mg tolvaptan, AUC and Cmax of plasma tolvaptan were less than doubled in patients with severe renal impairment relative to the controls. The peak increase in serum sodium was 5-6 mEq/L, regardless of renal function, but the onset and offset of tolvaptan's effect on serum sodium were slower in patients with severe renal impairment *[see Use in Special Populations (8.7)]*.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Up to two years of oral administration of tolvaptan to male and female rats at doses up to 1000 mg/kg/day (162 times the maximum recommended human dose [MRHD] on a body surface area basis), to male mice at doses up to 60 mg/kg/day (5 times the MRHD) and to female mice at doses up to 100 mg/kg/day (8 times the MRHD) did not increase the incidence of tumors.

Tolvaptan tested negative for genotoxicity in *in vitro* (bacterial reverse mutation assay and chromosomal aberration test in Chinese hamster lung fibroblast cells) and *in vivo* (rat micronucleus assay) test systems.

In a fertility study in which male and female rats were orally administered tolvaptan at 100, 300 or 1000 mg/kg/day, the highest dose level was associated with significantly fewer corpora lutea and implants than control.

13.3 Reproductive and Developmental Toxicology

In pregnant rats, oral administration of tolvaptan at 10, 100 and 1000 mg/kg/day during organogenesis was associated with a reduction in maternal body weight gain and food consumption at 100 and 1000 mg/kg/day, and reduced fetal weight and delayed ossification of fetuses at 1000 mg/kg/day (162 times the MRHD on a body surface area basis). Oral administration of tolvaptan at 100, 300 and 1000 mg/kg/day to pregnant rabbits during organogenesis was associated with reductions in maternal body weight gain and food consumption at all doses, and abortions at mid- and high-doses. At 1000 mg/kg/day (324 times the MRHD), increased incidences of embryo-fetal death, fetal microphthalmia, open eyelids, cleft palate, brachymelia and skeletal malformations were observed. There are no adequate and well-controlled studies of SAMSCA in pregnant women. SAMSCA should be used in pregnancy only if the potential benefit justifies the risk to the fetus.

14 CLINICAL STUDIES

14.1 Hyponatremia

In two double-blind, placebo-controlled, multi-center studies (SALT-1 and SALT-2), a total of 424 patients with euvolemic or hypervolemic hyponatremia (serum sodium <135 mEq/L) resulting from a variety of underlying causes (heart failure, liver cirrhosis, syndrome of inappropriate antidiuretic hormone [SIADH] and others) were treated for 30 days with tolvaptan or placebo, then followed for an additional 7 days after withdrawal. Symptomatic patients, patients likely to require saline therapy during the course of therapy, patients with acute and transient hyponatremia associated with head trauma or postoperative state and patients with hyponatremia due to primary polydipsia, uncontrolled adrenal insufficiency or uncontrolled hypothyroidism were excluded. Patients were randomized to receive either placebo (N = 220) or tolvaptan (N = 223) at an initial oral dose of 15 mg once daily. The mean serum sodium concentration at study entry was 129 mEq/L. Fluid restriction was to be avoided if possible during the first 24 hours of therapy to avoid overly rapid correction of serum sodium, and during the first 24 hours of therapy 87% of patients had no fluid restriction. Thereafter, patients could resume or initiate fluid restriction (defined as daily fluid intake of ≤1.0 liter/day) as clinically indicated.

The dose of tolvaptan could be increased at 24 hour intervals to 30 mg once daily, then to 60 mg once daily, until either the maximum dose of 60 mg or normonatremia (serum sodium >135 mEq/L) was reached. Serum sodium concentrations were determined at 8 hours after study drug initiation and daily up to 72 hours, within which time titration was typically completed. Treatment was maintained for 30 days with additional serum sodium assessments on Days 11, 18, 25 and 30. On the day of study discontinuation, all patients resumed previous therapies for hyponatremia and were reevaluated 7 days later. The primary endpoint for these studies was the average daily AUC for change in serum sodium from baseline to Day 4 and baseline to Day 30 in patients with a serum sodium less than 135 mEq/L. Compared to placebo, tolvaptan caused a statistically greater increase in serum sodium (p <0.0001) during both periods in both studies (see Table 2). For patients with a serum sodium of <130 mEq/L or <125 mEq/L, the effects at Day 4 and Day 30 remained significant (see Table 2). This effect was also seen across all disease etiology subsets (e.g., CHF, cirrhosis, SIADH/other).

SAMSCA® (tolvaptan)

Table 2. Effects of Treatment with Tolvaptan 15 mg/day to 60 mg/day

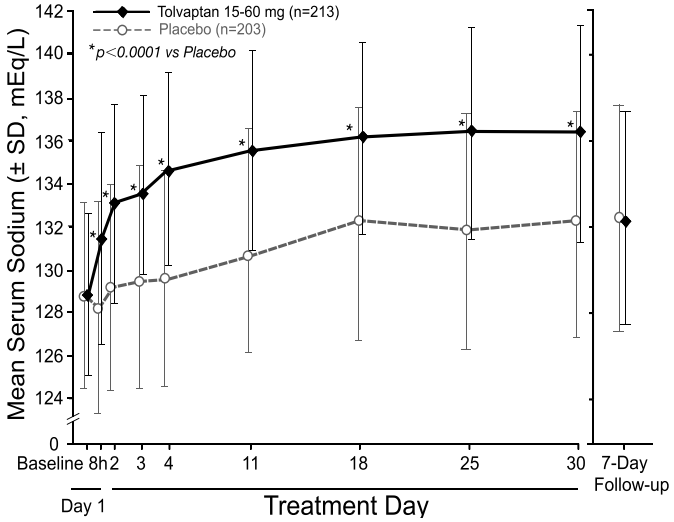
	Tolvaptan 15 mg/day-60 mg/day	Placebo	Estimated Effect (95% CI)
Subjects with Serum Sodium <135 mEq/L (ITT population)			
Change in average daily serum [Na+] AUC baseline to Day 4 (mEq/L) Mean (SD) N	4.0 (2.8) 213	0.4 (2.4) 203	3.7 (3.3-4.2) p <0.0001
Change in average daily serum [Na+] AUC baseline to Day 30 (mEq/L) Mean (SD) N	6.2 (4.0) 213	1.8 (3.7) 203	4.6 (3.9-5.2) p <0.0001
Percent of Patients Needing Fluid Restriction*	14% 30/215	25% 51/206	p =0.0017
Subgroup with Serum Sodium <130 mEq/L			
Change in average daily serum [Na+] AUC baseline to Day 4 (mEq/L) Mean (SD) N	4.8 (3.0) 110	0.7 (2.5) 105	4.2 (3.5-5.0) p <0.0001
Change in average daily serum [Na+] AUC baseline to Day 30 (mEq/L) Mean (SD) N	7.9 (4.1) 110	2.6 (4.2) 105	5.5 (4.4-6.5) p <0.0001
Percent of Patients Needing Fluid Restriction*	19% 21/110	36% 38/106	p <0.01
Subgroup with Serum Sodium <125 mEq/L			
Change in average daily serum [Na+] AUC baseline to Day 4 (mEq/L) Mean (SD) N	5.7 (3.8) 26	1.0 (1.8) 30	5.3 (3.8-6.9) p <0.0001
Change in average daily serum [Na+] AUC baseline to Day 30 (mEq/L) Mean (SD) N	10.0 (4.8) 26	4.1 (4.5) 30	5.7 (3.1-8.3) p <0.0001
Percent of Patients Needing Fluid Restriction*	35% 9/26	50% 15/30	p = 0.14

* Fluid Restriction defined as <1L/day at any time during treatment period.

In patients with hyponatremia (defined as <135 mEq/L), serum sodium concentration increased to a significantly greater degree in tolvaptan-treated patients compared to placebo-treated patients as early as 8 hours after the first dose, and the change was maintained for 30 days. The percentage of patients requiring fluid restriction (defined as ≤1 L/day at any time during the treatment period) was also significantly less (p =0.0017) in the tolvaptan-treated group (30/215, 14%) as compared with the placebo-treated group (51/206, 25%).

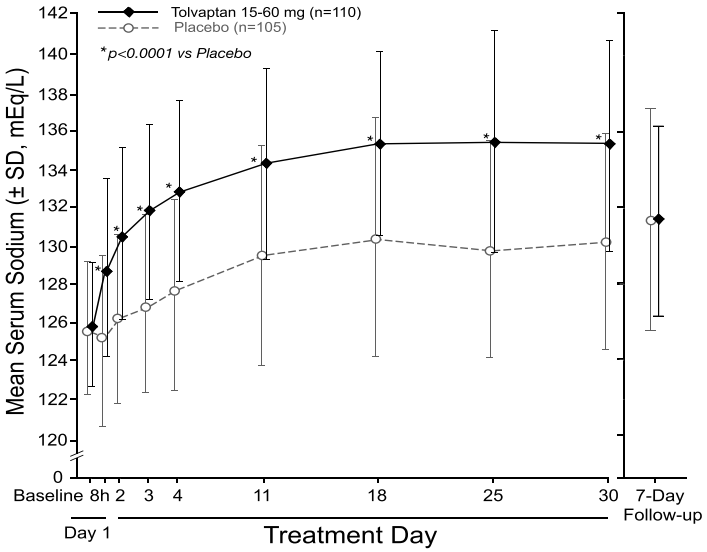
Figure 1 shows the change from baseline in serum sodium by visit in patients with serum sodium <135 mEq/L. Within 7 days of tolvaptan discontinuation, serum sodium concentrations in tolvaptan-treated patients declined to levels similar to those of placebo-treated patients.

Figure 1: Pooled SALT Studies: Analysis of Mean Serum Sodium (± SD, mEq/L) by Visit - Patients with Baseline Serum Sodium <135 mEq/L



*p-value <0.0001 for all visits during tolvaptan treatment compared to placebo

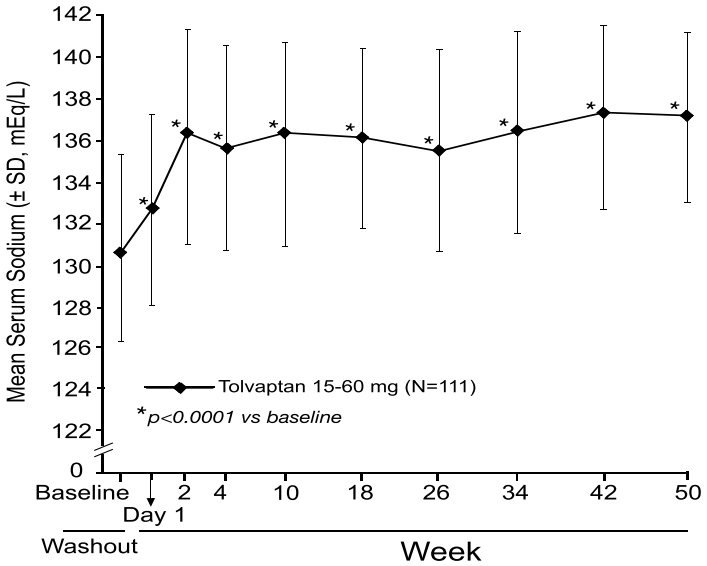
Figure 2: Pooled SALT Studies: Analysis of Mean Serum Sodium (± SD, mEq/L) by Visit - Patients with Baseline Serum Sodium <130 mEq/L



*p-value <0.0001 for all visits during tolvaptan treatment compared to placebo

In the open-label study SALTWATER, 111 patients, 94 of them hyponatremic (serum sodium <135 mEq/L), previously on tolvaptan or placebo therapy were given tolvaptan as a titrated regimen (15 to 60 mg once daily) after having returned to standard care for at least 7 days. By this time, their baseline mean serum sodium concentration had fallen to between their original baseline and post-placebo therapy level. Upon initiation of therapy, average serum sodium concentrations increased to approximately the same levels as observed for those previously treated with tolvaptan, and were sustained for at least a year. Figure 3 shows results from 111 patients enrolled in the SALTWATER Study.

Figure 3: SALTWATER: Analysis of Mean Serum Sodium (± SD, mEq/L) by Visit



*p-value <0.0001 for all visits during tolvaptan treatment compared to baseline

14.2 Heart Failure

In a phase 3 double-blind, placebo-controlled study (EVEREST), 4133 patients with worsening heart failure were randomized to tolvaptan or placebo as an adjunct to standard of care. Long-term tolvaptan treatment (mean duration of treatment of 0.75 years) had no demonstrated effect, either favorable or unfavorable, on all-cause mortality [HR (95% CI): 0.98 (0.9, 1.1)] or the combined endpoint of CV mortality or subsequent hospitalization for worsening HF [HR (95% CI): 1.0 (0.9, 1.1)].

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

SAMSCA® (tolvaptan) tablets are available in the following strengths and packages.

SAMSCA 15 mg tablets are non-scored, blue, triangular, shallow-convex, debossed with "OTSUKA" and "15" on one side.
Blister of 10 NDC 59148-020-50

SAMSCA 30 mg tablets are non-scored, blue, round, shallow-convex, debossed with "OTSUKA" and "30" on one side.
Blister of 10 NDC 59148-021-50

Storage and Handling

Store at 25 ºC (77 ºF), excursions permitted between 15 ºC and 30 ºC (59 ºF to 86 ºF) [see USP controlled Room Temperature].

Keep out of reach of children.

17 PATIENT COUNSELING INFORMATION

As a part of patient counseling, healthcare providers must review the SAMSCA Medication Guide with every patient *[see FDA-Approved Medication Guide]*.

Concomitant Medication

Advise patients to inform their physician if they are taking or plan to take any prescription or over-the-counter drugs since there is a potential for interactions.

Strong and Moderate CYP 3A inhibitors and P-gp inhibitors

Advise patients to inform their physician if they use strong (e.g., ketoconazole, itraconazole, clarithromycin, telithromycin, nelfinavir, saquinavir, indinavir, ritonavir) or moderate CYP 3A inhibitors (e.g., aprepitant, erythromycin, diltiazem, verapamil, fluconazole) or P-gp inhibitors (e.g., cyclosporine) *[see Dosage and Administration (2.3), Contraindications (4.4), Warnings and Precautions (5.5) and Drug Interactions (7.1)]*.

Nursing

Advise patients not to breastfeed an infant if they are taking SAMSCA *[see Use In Specific Populations (8.3)]*.

Manufactured by Otsuka Pharmaceutical Co., Ltd., Tokyo, 101-8535 Japan

Distributed and marketed by Otsuka America Pharmaceutical, Inc., Rockville, MD 20850

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Otsuka
Otsuka America Pharmaceutical, Inc.

07US17IBR0002 June 2017

MEDICATION GUIDE
SAMSCA® (sam-sca)
tolvaptan
Tablets

Read the Medication Guide that comes with SAMSCA before you take it and each time you get a new prescription. There may be new information. This Medication Guide does not take the place of talking to your healthcare provider about your medical condition or your treatment. Share this important information with members of your household.

What is the most important information I should know about SAMSCA?

1) **SAMSCA may make the salt (sodium) level in your blood rise too fast.** This can increase your risk of a serious condition called osmotic demyelination syndrome (ODS). ODS can lead to coma or death. ODS can also cause new symptoms such as:
   - trouble speaking
   - swallowing trouble or feeling like food or liquid gets stuck while swallowing
   - drowsiness
   - confusion
   - mood changes
   - trouble controlling body movement (involuntary movement) and weakness in muscles of the arms and legs
   - seizures

You or a family member should tell your healthcare provider right away if you have any of these symptoms even if they begin later in treatment. Also tell you healthcare provider about any other new symptoms while taking SAMSCA.

You may be more at risk for ODS if you have:
- liver disease
- not eaten enough for a long period of time (malnourished)
- very low sodium level in your blood
- been drinking large amounts of alcohol for a long period of time (chronic alcoholism)

To lessen your risk of ODS while taking SAMSCA:
- **Treatment with SAMSCA should be started and re-started only in a hospital, where the sodium levels in your blood can be checked closely.**
- Do not take SAMSCA if you can not tell if you are thirsty.
- To prevent losing too much body water (dehydration), have water available to drink at all times while taking SAMSCA. Unless your healthcare provider tells you otherwise, drink when you are thirsty.
- If your healthcare provider tells you to keep taking SAMSCA after you leave a hospital, it is important that you do not stop and re-start SAMSCA on your own. You may need to go back to a hospital to re-start SAMSCA. Talk to your healthcare provider right away if you stop taking SAMSCA for any reason.
- It is important to stay under the care of your healthcare provider while taking SAMSCA and follow their instructions.

2) **SAMSCA may cause liver problems, including life-threatening liver failure.** SAMSCA should not be taken for more than 30 days. Tell your doctor right away if you develop or have worsening of any of these signs and symptoms of liver problems:
   - Loss of appetite, nausea, vomiting
   - Fever, feeling unwell, unusual tiredness
   - Itching
   - Yellowing of the skin or the whites of the eyes (jaundice)
   - Unusual darkening of the urine
   - Right upper stomach area pain or discomfort

SAMSCA® (tolvaptan)

What is SAMSCA?

SAMSCA is a prescription medicine used to help increase low sodium levels in the blood, in adults with conditions such as heart failure, and certain hormone imbalances. SAMSCA helps raise salt levels in your blood by removing extra body water as urine.

It is not known if SAMSCA is safe or works in children.

Who should not take SAMSCA?

Do not take SAMSCA if:
- you are allergic to tolvaptan or any of the ingredients in SAMSCA. See the end of this Medication Guide for a complete list of ingredients in SAMSCA.
- the sodium level in your blood must be increased right away.
- you cannot replace fluids by drinking or you can not feel if you are thirsty.
- you are dizzy, faint, or your kidneys are not working normally because you have lost too much body fluid.
- you take certain medicines. These medicines could cause you to have too much SAMSCA in your blood:
  - the antibiotic medicines, clarithromycin (Biaxin, Biaxin XL) or telithromycin (Ketek)
  - the antifungal medicines, ketoconazole (Nizoral) or itraconazole (Sporonox)
  - the anti-HIV medicines, ritonavir (Kaletra, Norvir), indinavir (Crixivan), nelfinavir (Viracept), and saquinavir (Invirase)
  - the antidepressant medicine, nefazodone hydrochloride
- your body is not able to make urine. SAMSCA will not help your condition.

What should I tell my healthcare provider before taking SAMSCA?

Tell your healthcare provider about all your medical conditions, including if you:
- have kidney problems and your body can not make urine.
- have liver problems
- can not feel if you are thirsty. See "What is the most important information I should know about SAMSCA?"
- have any allergies. See the end of this Medication Guide for a list of the ingredients in SAMSCA.
- are pregnant or plan to become pregnant. It is not known if SAMSCA will harm your unborn baby.
- are breast-feeding. It is not known if SAMSCA passes into your breast milk. You and your healthcare provider should decide if you will take SAMSCA or breast-feed. You should not do both.
- are taking desmopressin (dDAVP).

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements.

Using SAMSCA with certain medicines could cause you to have too much SAMSCA in your blood. See "Who should not take SAMSCA?"

SAMSCA may affect the way other medicines work, and other medicines may affect how SAMSCA works.

Know the medicines you take. Keep a list of them and show it to your healthcare provider and pharmacist when you get a new medicine.

How should I take SAMSCA?

- See "What is the most important information I should know about SAMSCA?"
- Take SAMSCA exactly as prescribed by your healthcare provider.
- Take SAMSCA one time each day.
- You can take SAMSCA with or without food.
- Do not drink grapefruit juice during treatment with SAMSCA. This could cause you to have too much SAMSCA in your blood.
- Certain medicines or illnesses may keep you from drinking fluids or may cause you to lose too much body fluid, such as vomiting or diarrhea. If you have these problems, call your healthcare provider right away.
- Do not miss or skip doses of SAMSCA. If you miss a dose, take it as soon as you remember. If it is near the time of the next dose, skip the missed dose. Just take the next dose at your regular time. Do not take 2 doses at the same time.
- **If you take too much SAMSCA, call your healthcare provider right away.** If you take an overdose of SAMSCA, you may need to go to a hospital.
- If your healthcare provider tells you to stop taking SAMSCA, follow their instructions about limiting the amount of fluid you should drink.

What are the possible side effects of SAMSCA? SAMSCA can cause serious side effects including:

- **See "What is the most important information I should know about SAMSCA?"**
- **Loss of too much body fluid (dehydration).** Tell your healthcare provider if you:
  - have vomiting or diarrhea, and cannot drink normally.
  - feel dizzy or faint. These may be symptoms that you have lost too much body fluid.

Call your healthcare provider right away, if you have any of these symptoms.

The most common side effects of SAMSCA are:

- thirst
- dry mouth
- weakness
- constipation
- making large amounts of urine and urinating often
- increased blood sugar levels

These are not all the possible side effects of SAMSCA. Talk to your healthcare provider about any side effect that bothers you or that does not go away while taking SAMSCA.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

SAMSCA® (tolvaptan)

How should I store SAMSCA?

Store SAMSCA between 59 °F to 86 °F (15 °C to 30 °C).

Keep SAMSCA and all medicines out of the reach of children.

General Information about SAMSCA

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use SAMSCA for a condition for which it was not prescribed. Do not give SAMSCA to other people, even if they have the same symptoms you have. It may harm them.

This Medication Guide summarizes the most important information about SAMSCA. If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about SAMSCA that is written for healthcare professionals. For more information about SAMSCA, call 1-877-726-7220 or go to www.samsca.com.

What are the ingredients in SAMSCA?

Active ingredient: tolvaptan.

Inactive ingredients: corn starch, hydroxypropyl cellulose, lactose monohydrate, low-substituted hydroxypropyl cellulose, magnesium stearate and microcrystalline cellulose, and FD&C Blue No. 2 Aluminum Lake as colorant.

SAMSCA is a registered trademark of Otsuka Pharmaceutical Co., Ltd., Tokyo, 101-8535 Japan

Otsuka
Otsuka America Pharmaceutical, Inc. **07US14L-0919 Rev. 02, 2014**

This Medication Guide has been approved by the U.S. Food and Drug Administration.