NOVADOZ
AN MSN COMPANY

TOLVAPTAN TABLETS 15 mg and 30 mg

S.No.	Category	Question	Answer
Clinical Particulars			
1	Use/Indication	What is the product indicated for?	Tolvaptan tablets are 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).
2	Dosage	What is the recommended dosage?	Start with 15 mg once daily, and after at least 24 hours, increase to 30 mg once daily.
3	Administration	How do I take it?	The usual starting dose for tolvaptan tablets 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 tolvaptan tablets 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 tolvaptan tablets should be advised that they can continue ingestion of fluid in response to thirst
4	Formulation	Can tablet be crushed?	Do not crush or chew the tablets
5	Administration	What do I do if I miss a dose?	If you miss a dose of Tolvaptan tablets continue your prescribed course of therapy, and contact your physician immediately.
6	Administration	Use in Pediatric Population	Safety and effectiveness of tolvaptan in pediatric patients have not been established.
7	Administration	Use in Geriatric Population	Of the total number of hyponatremic subjects treated with tolvaptan in clinical studies, 42% were 65 years old and over, while 19% were 75 years old 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	Mechanism	Mechanism of Action	Tolvaptan is a selective vasopressin V2-receptor antagonist with a higher affinity for the V2-receptor (1.8 times that of AVP) and 29 times greater affinity for V2 than V1a. It promotes aquaresis by increasing urine water excretion, lowering urine osmolality, and raising serum sodium levels without significantly affecting sodium, potassium excretion, or plasma potassium concentrations. Its metabolites have little to no antagonist activity at V2-receptors.
9	Warning	Black Box Warning	WARNING: (A) INITIATE AND RE-INITIATE IN A HOSPITAL AND MONITOR SERUM SODIUM (B) NOT FOR USE FOR AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD) **(A) Initiate and re-initiate in a hospital and monitor serum sodium** **Tolvaptan 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.** **(B) Not for use for autosomal dominant polycystic kidney disease (ADPKD)** **Because of the risk of hepatotoxicity, tolvaptan should not be used for ADPKD outside of the FDA-approved REMS.**
10	Lactation	Use in Lactation	There are no data on tolvaptan or its metabolites in human milk or their effects on breastfed infants. Tolvaptan is present in rat milk, with concentrations

			reaching 1.5 to 15.8 times those in maternal blood. In rats, it caused increased perinatal death and reduced offspring body weight at doses 11 times the human maximum recommended dose (MRHD). Due to potential serious adverse effects, including electrolyte imbalances and volume depletion in infants, breastfeeding is not recommended during tolvaptan treatment.
11	Pregnancy	Use in Pregnancy	There is insufficient data on tolvaptan use in pregnant women to determine its risk for adverse developmental outcomes. Animal studies show no developmental toxicity in rats or rabbits at exposures 2.8 and 0.8 times the maximum recommended human dose (MRHD) of 60 mg. However, at higher doses, developmental effects were observed. In rats, delayed fetal ossification and reduced fetal weight occurred at 11 times the MRHD. In rabbits, teratogenic effects like microphthalmia and cleft palate were seen at 1.6 times the MRHD. The background risk for birth defects and miscarriage is 2-4% and 15-20%, respectively, in the general population. Due to potential risks, tolvaptan should be used during pregnancy only if the potential benefit justifies the risk.
12	Precautions	Is there any interaction between medication and alcohol?	No
13	Interaction	Is there any interaction with food?	tolvaptan may be administered with or without food.
14	Side effects	What are the common side effects?	**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 tolvaptan tablets are: thirst • dry mouth • weakness • constipation • making large amounts of urine and

			urinating often • increased blood sugar levels
15	Storage	What are the storage conditions?	Store tolvaptan tablets between 59°F to 86°F (15°C to 30°C).
16	Dispensing	How to Dispense?	As prescribed by the Physician
17	Contraindication	What are the contraindications of (medication).	**Tolvaptan tablets are contraindicated in the following conditions:** • Patients with autosomal dominant polycystic kidney disease (ADPKD) outside of FDA-approved REMS • Unable to sense or respond to thirst • Hypovolemic hyponatremia • Taking strong CYP3A inhibitors • Anuria • Hypersensitivity (e.g., anaphylactic shock, rash generalized) to tolvaptan or any components of the product .
Pharmaceutical Particulars			
18	Pharmaceutical Form	How is it supplied?	**How Supplied** Tolvaptan tablets are available in the following strengths and packages. Tolvaptan tablets 15 mg are light blue to blue colored, triangle, biconvex, uncoated tablets, debossed with "MT" on one side and "7" on other side, free from physical defects. Carton of 10 tablets (1 x 10 unit-dose) NDC 72205-130-11 Tolvaptan tablets 30 mg are light blue to blue colored, round, biconvex, uncoated tablets, debossed with "MT" on one side and "8" on other side, free from physical defects. Carton of 10 tablets (1 x 10 unit-dose) NDC 72205-131-11
19	Ingredients	Active and Inactive Ingredients	**Active**: tolvaptan. **Inactive** corn starch, croscarmellose sodium, hydroxypropyl cellulose, lactose monohydrate, magnesium stearate, microcrystalline cellulose, and FD&C Blue No. 2 Aluminum Lake as colorant. This Medication Guide has been approved by the U.S. Food and Drug Administration.
20	Coating	What is the type of coating?	Uncoated tablets

Allergens			
21	Ingredients	Is it Vegetarian?	No
22	Ingredients	Does it contain Gluten?	No
23	Ingredients	Does it contain Dairy Products?	Yes
24	Ingredients	Does it contain Casein	No
25	Ingredients	Does it contain Whey?	No
26	Ingredients	Does it contain corn?	Yes
27	Ingredients	Does it contain rye?	No
28	Ingredients	Does it contain sugar?	No
29	Ingredients	Does it contain Oats?	No
30	Ingredients	Does it contain wheat?	No
31	Ingredients	Does it contain spelt?	No
32	Ingredients	Does it contain barley?	No
33	Ingredients	Does it contain rennet?	No
34	Ingredients	Does it contain starch?	No
36	Ingredients	Does it contain Iodine?	No
37	Ingredients	Does it contain latex?	No
38	Ingredients	Does it contain alcohol?	Yes
39	Ingredients	Does it contain dyes?	Yes
40	Ingredients	Does it contain flavor?	No
41	Ingredients	Does it contain Lactose?	Yes
42	Ingredients	Does it contain Nuts?	No
43	Ingredients	Does it contain Preservatives?	No
44	Ingredients	Does it contain Soy products?	No
45	Ingredients	Does it contain peanut?	No

46	Ingredients	Does it contain nickel?	No
Miscellaneous			
47	Miscellaneous	May I know the product availability?	Novadoz Pharmaceuticals products are only available through pharmacies, wholesalers, and other authorized distributors. See our ADR (authorized distributors of record) page at NovadozPharma.com to learn more about where to find our products.
48	Miscellaneous	May I know about return, refunds and reimbursement?	Contact Novadoz Pharmaceuticals Customer Service directly at 908-360-1500
49	Miscellaneous	Do you have any patient's assistance program?	Novadoz Pharmaceuticals does not offer patient assistance programs at this time. The company that produces the brand version of your product may or may not offer such a program. Please check for access & eligibility requirements with that company.
50	Miscellaneous	How do I report an adverse drug effect or reaction to Novadoz medication?	To report suspected adverse reactions, contact Novadoz Pharmaceuticals LLC at 1-855-668-2369 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.
51	Miscellaneous	Why does my pharmacy that used to fill your generic formulation of a particular medicine, no longer fills my prescription with Novadoz formulation?	Please check with your pharmacy as to why your prescription is not a Novadoz Pharmaceuticals product. You may refer to NovadozPharma.com ADR (authorized distributor of record) page to learn where to find our products.
52	Miscellaneous	Manufacturer and Distributor	**Manufactured by:** **MSN Laboratories Private Limited** Telangana – 509 228, INDIA **Distributed by:** **Novadoz Pharmaceuticals LLC** Piscataway, NJ 08854-3714