Summary of Clinical Evidence

Tolvaptan is indicated to slow kidney function decline in adults at risk of rapidly progressing ADPKD. Changes in surrogate markers (e.g., eGFR) demonstrate that tolvaptan slows progression of renal disease in patients with ADPKD. However, tolvaptan is not tolerated by all patients. The efficacy of tolvaptan in patients with ADPKD without preexisting hypertension is unknown. The most common adverse events in patients treated with Jynarque (incidence > 10% and at least twice that for placebo) were thirst, polyuria, nocturia, pollakiuria, and polydipsia.

Samsca (tolvaptan) is an oral non-peptide V2 vasopressin receptor antagonist indicated for the treatment of clinically significant hypervolemic and euvolemic hyponatremia (i.e., serum sodium < 125 mEq/L or less marked hyponatremia that is symptomatic and has resisted correction with fluid restriction), including in members with heart failure, cirrhosis, and syndrome of inappropriate antidiuretic hormone (SIADH). Tolvaptan is initiated and re-initiated in a hospital and then continued on an out-member basis and has been shown to induce short-term clinical improvements but has not demonstrated improvement in long-term outcomes such as mortality or hospitalizations.
Agents known to cause hyponatremia (not an all-inclusive list): amiodarone, antipsychotics, amitriptyline, bromocriptine, carbamazepine, ciprofloxacin, cisplatin, chlorpropamide, clofibrate, cyclophosmamide, desmopressin, haloperidol, ifosfamide, imatinib (high doses) interferon-alpha, interferon-gamm lorcainide, melphalan, methotrexate, monoamine oxidase inhibitors, nicotine, narcotics, NSAIDs, opiate, selective serotonin reuptake inhibitors (SSRIs), sodium valproate, thioridazine, thiothixene, tricyclic antidepressants, vasopressin, vinblastine, vincristine, vinorelbine

Jynarque REMS Program

JYNARQUE is available only through a restricted distribution program under a Risk Evaluation and Mitigation Strategy (REMS) called the JYNARQUE REMS Program, because of the risks of liver injury. Notable requirements of the JYNARQUE REMS Program include the following:

- Prescribers must be certified by enrolling in the REMS program.
- Prescribers must inform patients receiving JYNARQUE about the risk of hepatotoxicity associated with its use and how to recognize the signs and symptoms of hepatotoxicity and the appropriate actions to take if it occurs.
- Patients must enroll in the REMS program and comply with ongoing monitoring requirements.
- Pharmacies must be certified by enrolling in the REMS program and must only dispense to patients who are authorized to receive JYNARQUE.

Further information, including a list of qualified pharmacies/distributors, is available at www.JYNARQUEREMS.com or by telephone at 1-877-726-7220.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of tolvaptan are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Jynarque (tolvaptan) include: history of signs or symptoms of significant liver impairment or injury, concomitant use of strong CYP3A inhibitors (e.g., clarithromycin, ketoconazole, itraconazole, ritonavir, indinavir, nelfinavir, saquinavir, nefazodone, telithromycin), unable to sense or respond to thirst, uncorrected abnormal blood sodium concentrations (particularly hypernatremia), hypovolemia, concomitant use of diuretics, uncorrected urinary outflow obstruction, anuria, hypersensitivity to tolvaptan or any of its components. Contraindications to Samsca (tolvaptan) include: Use in patients with autosomal dominant polycystic kidney disease (ADPKD) outside of FDA-approved REMS; concomitant use of strong of CYP3A inhibitors (e.g., clarithromycin, ketoconazole, itraconazole, ritonavir, indinavir, nelfinavir, saquinavir, nefazodone, telithromycin), unable to respond appropriately to thirst, hypovolemic hyponatremia, anuria, hypersensitivity.

OTHER SPECIAL CONSIDERATIONS:

Jynarque (tolvaptan) has a BLACK BOX WARNING for risk of serious liver injury. JYNARQUE (tolvaptan) can cause serious and potentially fatal liver injury. Acute liver failure requiring liver transplantation has been reported. Measure transaminases and bilirubin before initiating treatment, at 2

weeks and 4 weeks after initiation, then continuing monthly for the first 18 months and every 3 months thereafter. JYNARQUE is available only through a restricted distribution program called the JYNARQUE REMS Program.

Samsca (tolvaptan) has a BLACK BOX WARNING for A) initiate and re-initiate in a hospital and monitor serum sodium and B) not for use for autosomal dominant polycystic kidney disease (ADPKD). A) 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. B) Because of the risk of hepatotoxicity, tolvaptan (Samsca) should not be used for autosomal dominant polycystic kidney disease (ADPKD) outside of the FDA-approved REMS.

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Jynarque TABS 15MG
Jynarque TABS 30MG
Jynarque TBPK 15MG
Jynarque TBPK 30 & 15MG
Jynarque TBPK 45 & 15MG
Jynarque TBPK 60 & 30MG
Jynarque TBPK 90 & 30MG
Samsca TABS 15MG
Samsca TABS 30MG
Tolvaptan TABS 15MG
Tolvaptan TABS 30MG

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SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Duration of Approval Prescriber Requirements Quantity Background Contraindications/Exclusions/Discontinuation Other Special Considerations Available Dosage Forms	Q3 2023
REVISION- Notable revisions: Continuation of Therapy Quantity Contraindication/Exclusions/Discontinuation	Q2 2022
Q2 2022 Established tracking in new format	Historical changes on file