| Patient name | | Patient hospital number | |
|---|---|---|---|

# JINARC®▼ (tolvaptan) Prescribing Checklist For Treatment Initiation

JINARC® (tolvaptan) is indicated to slow the progression of cyst development and renal insufficiency of autosomal dominant polycystic kidney disease (ADPKD) in adults with CKD stage 1 to 4 at initiation of treatment and evidence of rapidly progressing disease. This checklist should be used before treatment initiation (**Sections A** and **B**) and during ongoing treatment (**Section C**) with JINARC®.

## Section A: Check patient's eligibility for initiating Jinarc® treatment

**For the following statements, please tick 'Yes' if the statement applies to the patient, or 'No' if it does not**

| **CONTRAINDICATIONS** – if any of the following apply to the patient then they should **not** be treated with JINARC® | **Yes** | **No** |
|---|---|---|
| Elevated liver enzymes as follows:<br>• ALT or AST >8 x upper limit of normal (ULN);<br>• ALT or AST >5 x ULN for more than 2 weeks;<br>• ALT or AST >3 x ULN and (BT >2 x ULN or international normalized ratio [INR] >1.5)<br>• ALT or AST >3 x ULN with persistent symptoms of hepatic injury (such as fatigue, anorexia, nausea, right upper abdominal discomfort, vomiting, fever, rash, pruritus, dark urine or jaundice) | | |
| Hypersensitivity to the active substance or any of its excipients (e.g. lactose or galactose intolerance, benzazepine or benzazepine derivatives) | | |
| Anuria | | |
| Volume depletion | | |
| Hypernatraemia | | |
| Inability to perceive or respond to thirst | | |
| Trying for a pregnancy, Pregnant or breastfeeding | | |
| Unwilling/unable for monthly monitoring visits | | |
| **PRECAUTIONARY CONDITIONS** –<br>If any of the following apply to the patient, caution along with appropriate monitoring should be used | **Yes** | **No** |
| Raised liver enzymes, AST and/or ALT stabilised at no greater than 3 x ULN<br>**In case of abnormal baseline levels below the limits for permanent discontinuation, treatment can only be initiated if the potential benefits of treatment outweigh the potential risks and liver function testing must continue at increased time frequency. The advice of a hepatologist is recommended.** | | |
| Severe hepatic impairment (Child-Pugh class C) | | |
| Limited access to water and signs of dehydration | | |
| Partial obstruction of urinary outflow (e.g. prostatic hypertrophy) | | |
| Fluid and electrolyte imbalance | | |
| Serum sodium abnormalities | | |
| History of anaphylaxis | | |
| Lactose and galactose intolerance | | |
| Diabetes Mellitus | | |
| Elevated uric acid concentration | | |
| Decreased glomerular filtration rate | | |
| Use of medicines likely to interact with Jinarc® such as CYP3A inhibitors (e.g. ketoconazole, fluconazole, grapefruit juice), CYP3A inducers (e.g. rifampin), CYP3A substrates, transporter substrates, digoxin, drugs increasing serum sodium concentration, diuretics or non-diuretic anti-hypertensive medicinal products, and vasopressin analogues. *Jinarc® is to be administered in daily doses of 15mg or 30mg in patients taking drugs that are moderate or strong CYP 3A inhibitors, as concomitant use of these drugs increases Jinarc® exposure. Please see Jinarc SmPC for detailed information. (See Jinarc SmPC, Sections 4.2 and 4.5 for the complete information)* | | |
| **PRESCRIBING DECISION (Initiation)** | **Yes** | **No** |

| | | |
|---|---|---|
| **I intend to initiate treatment with JINARC® (select one dose below):**<br>○ 60mg per day (split dose 45mg and 15mg)<br>○ Split dose 15mg and 15mg (if patient is also on moderate CYP3A inhibitor)<br>○ 15mg per day (if patient is also on strong CYP3A inhibitor) | | |
| If you have decided to prescribe JINARC® please complete **Section B** | | |

## Section B: Patient education

**Please tick the corresponding box if the statement applies to the patient**

| | | | |
|---|---|---|---|
| **I have reminded the patient** of the risk of liver toxicity with use of Tolvaptan therapy, need for monthly blood liver function test for the first 18 months of therapy and 3 monthly thereafter on continuing therapy. | | | |
| **I have reminded the patient** to be vigilant for signs and symptoms of hepatic injury, to drink adequate fluids ahead of thirst sensation and to drink 1-2 glasses of fluid before bedtime. | | | |
| **I have advised a female patient** to use adequate contraception and to report pregnancy if it occurs while on treatment.<br>**Or the patient is male or a woman of non-childbearing potential** | | | |
| **I have given the patient** a Patient Education Brochure and Patient Alert Card. | | | |
| **Prescriber signature** | | **Date** | |

| Patient name | | Patient hospital number | |
|---|---|---|---|

# JINARC®▼ (tolvaptan) Prescribing Checklist For Patient Monitoring

## Section C: Check patient's on-going eligibility for Jinarc® treatment

The following sections should be completed monthly for Jinarc® (tolvaptan) patients who are being treated for ADPKD for the first 18 months, and then every 3 months thereafter**.**

**All adverse events should be reported to Otsuka using the reporting mechanism below.**

**Please tick 'Yes' if the statement applies to the patient, 'No' if it does not**

| **HEPATIC INJURY** | **Yes** | **No** |
|---|---|---|
| **Is the patient showing any signs or symptoms of liver injury** (fatigue, anorexia, nausea, right upper abdominal discomfort, vomiting, fever, rash, pruritus, icterus, dark urine or jaundice)**? If the answer is Yes, treatment with Jinarc® should be stopped, the cause investigated and the occurrence reported using the reporting mechanisms below.** | | |

| **Liver function test results** | **Recommended action** |
|---|---|
| ALT or AST abnormal | **Stop Jinarc® treatment and investigate the cause of the raised liver enzyme(s) including repeat tests as soon as possible (ideally within 48-72 hours). Report decision to Otsuka using the reporting mechanism below. Continue monitoring.** |
| Liver Function results stabilise<br>If ALT and AST levels remain below 3 x ULN | **Re-start Jinarc® treatment cautiously at same or lower dose with frequent monitoring and report decision to Otsuka using the reporting mechanism below** |
| ALT or AST >8-times ULN | **Permanently discontinue treatment and report decision to Otsuka using the reporting mechanisms below.** |
| ALT or AST >5-times ULN for more than 2 weeks | |
| ALT or AST >3-times ULN and (BT >2-times ULN or International Normalized Ratio [INR] >1.5) | |
| ALT or AST > 3-times ULN with persistent symptoms of hepatic injury (such as fatigue, anorexia, nausea, right upper abdominal discomfort, vomiting, fever, rash, pruritus, dark urine or jaundice). | |

| **PRESCRIBING DECISION (On-going treatment)**<br>**Titrate dose upward, if tolerated, with at least weekly intervals between up-titrations.** | |
|---|---|
| **Based on tolerability and other tests performed on this patient (select one option below)** | |
| • **I intend to prescribe Jinarc® (select one dose below)** | |
| ○ 15mg (for patients also taking strong CYP3A inhibitors) | |
| ○ 30mg (for patients also taking strong CYP3A inhibitors) | |
| ○ 30mg per day (15mg and 15mg split dose) for patients also taking moderate CYP3A inhibitors<br>○ 45mg per day (30mg and 15mg split dose) for patients also taking moderate CYP3A inhibitors<br>○ 60mg per day (45mg and 15mg split dose) for patients also taking moderate CYP3A inhibitors<br>○ 60mg per day (45mg and 15 mg split dose) | |
| ○ 90mg per day (60mg and 30mg split dose) | |
| ○ 120mg per day (90mg and 30mg split dose) | |
| • **I have decided to interrupt treatment** | |
| • **I have decided to permanently discontinue treatment** | |
| ○ Liver function contraindications | |
| ○ Patient has been lost to follow-up | |
| ○ Patient has died | |
| ○ Patient choice | |
| ○ Other | |

| | | | |
|---|---|---|---|
| **Prescriber signature** | | **Date** | |

**Please report Adverse Drug Reactions to local representative of MAH, Swixx Biopharma S.M.S.A. Pharmacovigilance Department on telephone: +30 214 444 9670 (including out of hours) or by email: medinfo.malta@swixxbiopharma.com, and to the Medicines Authority ADR reporting form, which is available online at http://www.medicinesauthority.gov.mt/adrportal , and sent by post or email to: P: Pharmacovigilance Section at Post-Licensing Directorate, Medicines Authority, Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000 E: postlicensing.medicinesauthority@gov.mt**