# Medicines Management Programme

# Managed Access Protocol – Tolvaptan for the treatment of autosomal dominant polycystic kidney disease

| Medicine | Date of addition to Managed Access Protocol |
|---|---|
| **Tolvaptan (Jinarc®)** | 28/02/2020 |

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| **Approved by** | **Professor Michael Barry, Clinical Lead, MMP** | |
| **Date approved** | Version 1.0 | 28/02/2020 |
| **Date updated** | Version 1.1 | 29/11/2022 |
| | Version 1.2 | 10/06/2025 |

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|---|---|
| ADPKD | Autosomal dominant polycystic kidney disease |
| CKD | Chronic kidney disease |
| CKD-EPI | Chronic Kidney Disease Epidemiology Collaboration |
| eGFR | Estimated glomerular filtration rate |
| GFR | Glomerular filtration rate |
| HSE | Health Service Executive |
| HTH | High Tech Hub |
| MAP | Managed access protocol |
| MDRD | Modification of Diet in Renal Disease |
| mGFR | Measured glomerular filtration rate |
| MMP | Medicines Management Programme |
| PCRS | Primary Care Reimbursement Service |
| REPRISE | Replicating Evidence of Preserved Renal Function: an Investigation of Tolvaptan Safety and Efficacy in ADPKD |
| SmPC | Summary of Product Characteristics |
| TEMPO | Tolvaptan Efficacy and Safety in Management of Autosomal Dominant Polycystic Kidney Disease and Its Outcomes |


## Acknowledgements

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# 1. Tolvaptan for the treatment of autosomal dominant polycystic kidney disease

Jinarc® contains tolvaptan. Tolvaptan is a vasopressin antagonist that specifically blocks the binding of arginine vasopressin at the V2 receptors of the distal portions of the nephron.

From 01 July 2019, five presentations of tolvaptan are available on the High Tech Arrangement:

- Jinarc® 15 mg Tablets (7 Tablets)
- Jinarc® 30 mg Tablets (7 Tablets)
- Jinarc® (45 mg x 28 & 15 mg x 28) Tablets (56 Tablets)
- Jinarc® (60 mg x 28 & 30 mg x 28) Tablets (56 Tablets)
- Jinarc® (90 mg x 28 & 30 mg x 28) Tablets (56 Tablets).

## 1.1 Licensed indication

Tolvaptan (Jinarc®) is indicated to slow the progression of cyst development and renal insufficiency of autosomal dominant polycystic kidney disease (ADPKD) in adults with chronic kidney disease (CKD) stage 1 to 4 at initiation of treatment with evidence of rapidly progressing disease.

## 1.2 Reimbursement

Reimbursement of tolvaptan on the High Tech Arrangement for the treatment of ADPKD is supported only for adults with CKD stage 2 or 3 at initiation of treatment with evidence of rapidly progressing disease, who meet the criteria outlined in this Managed Access Protocol (MAP). All criteria must be satisfied in order for reimbursement to be supported.

An application for reimbursement approval is required to be submitted on an individual patient basis. The *Tolvaptan (Jinarc®) Application Form* should be completed and sent by secure email to the Health Service Executive (HSE)-Medicines Management Programme (MMP) at mmp@hse.ie.

Table 1 outlines the licensed therapeutic dosage of tolvaptan for ADPKD. Please refer to the Summary of Product Characteristics (SmPC) for further prescribing information.

**Table 1 Licensed therapeutic dosage of tolvaptan (Jinarc®)**

| Medicine | Route of administration | Starting dosage | Maximum dosage |
|---|---|---|---|
| **Tolvaptan** | Oral | 45 mg in the morning and 15 mg eight hours after the morning dose | 90 mg in the morning and 30 mg eight hours after the morning dose |

mg: milligrams

If a patient is recommended for reimbursement of tolvaptan, reimbursement is supported up to the maximum licensed dosage specified in Table 1. Reimbursement of dosages in excess of the licensed therapeutic dosages (as outlined in Table 1) is not supported.

See Section 3 for further details on Reimbursement criteria – Requirement for outcome data.

## 1.3 Reimbursement price

The reimbursement prices of the presentations of tolvaptan available on the High Tech Arrangement are outlined in Table 2. Commercial-in-confidence arrangements are in place with the marketing authorisation holders to reduce the net acquisition cost of tolvaptan to the HSE.

**Table 2 Reimbursement codes and prices for the presentations of tolvaptan available on the High Tech Arrangement**

| Strength (pack size) | Code | Reimbursement price* |
|---|---|---|
| **Jinarc® Tablets 15 mg (7)** | 88943 | €362.71 |
| **Jinarc® Tablets 30 mg (7)** | 88944 | €367.80 |
| **Jinarc® Tablets 45 mg & 15 mg (56)** | 88940 | €1,382.93 |
| **Jinarc® Tablets 60 mg & 30 mg (56)** | 88941 | €1,396.95 |
| **Jinarc® Tablets 90 mg & 30 mg (56)** | 88942 | €1,410.90 |

mg: milligrams
*Correct as at 01/06/2025

## 2. Reimbursement criteria - Initiation

This section outlines the criteria that must be satisfied in order for a patient to be recommended for reimbursement of tolvaptan for ADPKD under the High Tech Arrangement.

### 2.1 Prescribers

Applications for reimbursement approval for tolvaptan for the treatment of ADPKD under the High Tech Arrangement will only be considered from consultants with specialist registration with the Irish Medical Council in a specialism relevant to the management of ADPKD (i.e. nephrology), who have agreed to the terms of this MAP and been approved by the HSE ('approved consultants').

Approved consultants are responsible for ensuring that the patient or their representative/guardian is aware that the application for reimbursement approval is being made on their behalf.

The prescribing of Jinarc® for approved patients for the treatment of ADPKD under the High Tech Arrangement will be confined to the approved consultants and their teams. The governance of the team on the High Tech Hub, including access, rests with the approved consultant.

### 2.2 Patient age

Applications for reimbursement approval will only be considered for individuals aged 18 - 55 years at time of application. As per the SmPC, only limited data on the safety and effectiveness of tolvaptan in ADPKD patients aged over 55 years are available.

### 2.3 Patient diagnosis

In line with the TEMPO 3:4 and REPRISE trials, the information contained within the SmPC and the 2021 European consensus statement update[i] on the use of tolvaptan for ADPKD, the reimbursement criteria for initiation of tolvaptan (Jinarc®) are:

- Diagnosis of ADPKD,
- CKD stage 2 or 3, and
- Evidence of rapidly progressing disease.

For reimbursement approval, clinicians will be required to confirm the diagnosis of ADPKD at the time of application.

[i] Müller RU, Messchendorp AL, Birn H et al. An update on the use of tolvaptan for autosomal dominant polycystic kidney disease: consensus statement on behalf of the ERA Working Group on Inherited Kidney Disorders, the European Rare Kidney Disease Reference Network and Polycystic Kidney Disease International. *Nephrol Dial Transplant* 2022; 37(5): 825-839.

### 2.3.1 Confirmed diagnosis of autosomal dominant polycystic kidney disease

A diagnosis of ADPKD can be established:

- in patients with a family history: age-related modified Pei-Ravine imaging (Table 3) or
- in patients without a family history: more than 10 cysts per kidney (using any imaging method) and exclusion of other forms of cystic kidney disease.

**Table 3 Unified ultrasound age-related modified Pei-Ravine imaging criteria**

| Age (years) | Diagnostic criteria |
|---|---|
| **15 - 29** | ≥ 3 cysts (total) |
| **30 - 39** | ≥ 3 cysts (total) |
| **40 - 59** | ≥ 2 cysts (each kidney) |

These criteria are only valid in patients with a positive family history and are specific for ultrasound imaging only.

### 2.3.2 Chronic kidney disease stage 2 or 3

Similar to other chronic kidney diseases, ADPKD is typically staged by renal function status. The estimated glomerular filtration rate (eGFR) measurements corresponding to each stage are shown in Table 4 below. Reimbursement will only be supported for ADPKD patients with CKD stage 2 or 3 at initiation of treatment (i.e. eGFR 30 - 89 ml/min/1.73 $m^2$).

**Table 4 Classification of chronic kidney disease by estimated glomerular filtration rate**

| Stage | Description | eGFR (ml/min/1.73 $m^2$) |
|---|---|---|
| **1** | Kidney damage with normal or increased eGFR | ≥ 90 |
| **2** | Kidney damage with mild decrease in eGFR | 60 - 89 |
| **3a** | Moderate decrease in eGFR | 45 - 59 |
| **3b** | Moderate decrease in eGFR | 30 - 44 |
| **4** | Severe decrease in eGFR | 15 - 29 |
| **5** | Kidney Failure | < 15 or dialysis |

eGFR: estimated glomerular filtration rate

In the application for reimbursement approval, glomerular filtration rate (GFR) should be estimated by either the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation or the Modification of Diet in Renal Disease (MDRD) study equation.

The following patient measurements must be provided in the application for reimbursement approval:

- Weight
- Height
- Serum creatinine
- Estimated GFR ($eGFR_{MDRD}$ or $eGFR_{CKD\text{-}EPI}$).

The following patient measurement can be provided in the application for reimbursement approval:

- Measured GFR (mGFR) i.e. 24-hour urine clearance or by isotope method.

When reviewing applications, the MMP may request this measurement as additional information to support the staging of CKD.

All measurements should be taken in the six week period prior to date of application.

### 2.3.3 Evidence of rapidly progressing disease

Evidence to support rapid progression of ADPKD must be included in the application for reimbursement approval. A historical fast eGFR decline, with no other confounding cause than ADPKD is a marker of rapid disease progression.

Rapid disease progression in ADPKD can be defined as a sustained decline in eGFR of ≥ 3 ml/min/1.73m$^2$ per year over a period of four years or greater.

- At least five measurements over a period of at least four years must be provided.
- The date of the first and last eGFR measurement must be at least four years apart.
- Measurements must be provided for at least three individual years during this period.
- The date of the most recent measurement must be within the six week period prior to date of application.

Clinicians are required to provide copies of lab reports to confirm eGFR measurements.

## 2.4 Patient clinical history

In line with the SmPC for Jinarc®, applications for reimbursement approval will not be considered for individuals who meet any of the contraindications for treatment as outlined in the SmPC.

# 3. Reimbursement criteria – Requirement for outcome data

Follow-up data may be requested by the MMP for audit purposes and provision of same is a condition of ongoing reimbursement. It is the responsibility of the approved consultant to ensure that the patient or their representative/guardian is aware that the provision of follow-up data is a condition of reimbursement, and that audits may occur during which their personal data will be reviewed.

## 4. Reimbursement – Discontinuation

### 4.1 Chronic kidney disease stage 4

Although reimbursement is not supported for patients with CKD stage 4 on initiation, approved patients who progress to stage 4 will receive ongoing reimbursement support.

### 4.2 Chronic kidney disease stage 5

The SmPC states that patients should discontinue tolvaptan treatment if renal insufficiency progresses to CKD stage 5, therefore reimbursement will no longer be supported if a patient progresses to stage 5.

## 5. Prescribing of tolvaptan for approved patients

Please refer to the SmPC for Jinarc® for full prescribing information including monitoring and patient counselling requirements.

If a patient is recommended for reimbursement by the MMP, the high tech prescription should be generated on the High Tech Hub (HTH). High tech prescriptions that are not hub generated for Jinarc® will not be eligible for reimbursement by the HSE Primary Care Reimbursement Service (PCRS). Only approved consultants and their teams will have access to generate prescriptions.