# Okedi®

Risperidone prolonged-release suspension for injection 75 mg, 100 mg

**OKEDI® is indicated for the treatment of schizophrenia in adults for whom tolerability and effectiveness have been established with oral risperidone[1]**

# A DISTINCTIVE PATH FOR YOUR PATIENTS FROM DAY 1[1,2]

**No need for oral supplementation or loading doses which may improve the therapeutic alliance[1,3]**

Prescribing information can be found at the end of this document
UK-OKE-23-11/0004. January 2024

ROVI

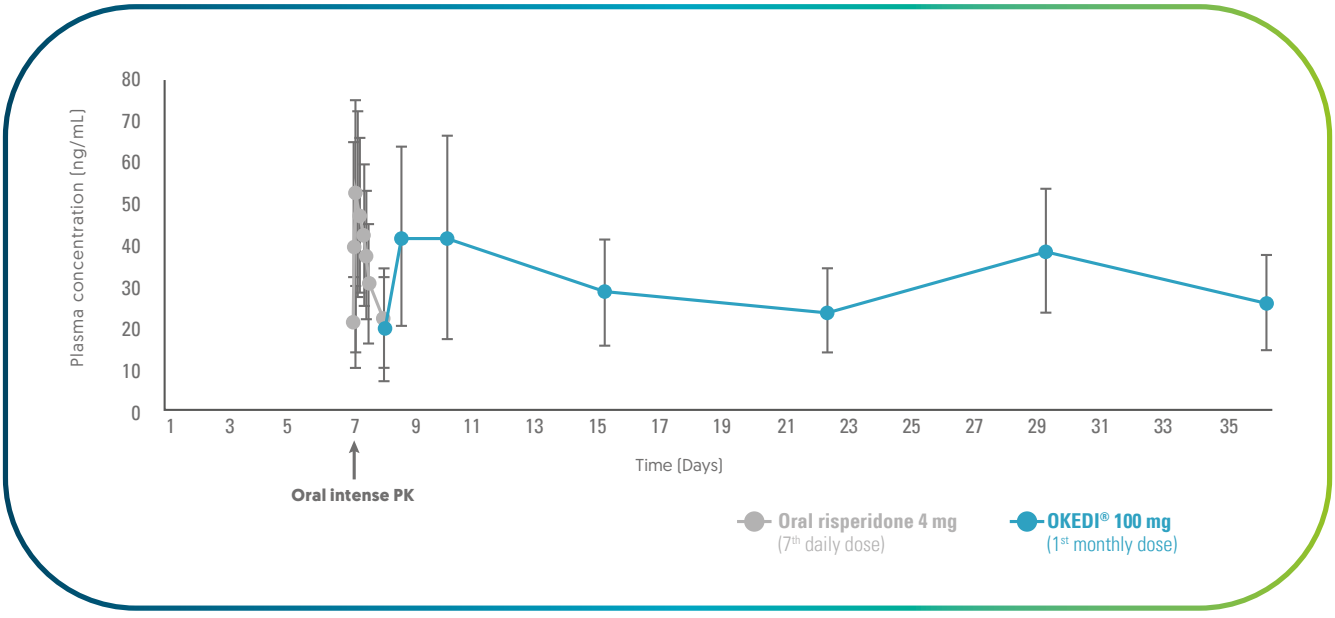
# OKEDI®, with innovative ISM® technology, is a convenient 4-weekly long-acting injectable antipsychotic from ROVI

# INDICATED FOR THE TREATMENT OF SCHIZOPHRENIA IN ADULTS

for whom tolerability and effectiveness have been established with oral risperidone[1]

**Effective and generally well tolerated 4-weekly risperidone LAI developed to offer a convenient path for your patients from Day 1[1,2]**

**OKEDI®** rapidly achieves **therapeutic plasma levels on Day 1**, which are **sustained throughout the dosing period** without the need for loading doses or oral supplementation.[1,5]




Mean (±SD) plasma concentrations versus time profiles for risperidone active moiety during oral risperidone 4 mg treatment (7th dose) and after switching to OKEDI® 100 mg (PK population). Notes: Once daily oral risperidone 4 mg was administered for 7 days. An intense oral pharmacokinetic (PK) analysis was conducted at study Day 7 (last day of the oral risperidone treatment) including samples at pre-dose (within 0.5 hours relative to the dose time), 1, 2, 3, 4, 6, 8, and 12 hours, post-dose (grey line). Twenty-four hours after the last oral risperidone dose (study Day 8), a single intramuscular dose of OKEDI® 100 mg was administered and PK samples were obtained at pre-dose and 12 hours post-dose, as well as at Days 10, 15, 22, 29, and 36 (blue line).[5]

**LAI:** Long-Acting Injectable; **SD**: Standard Deviation.

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## Immediate release of OKEDI®, achieving similar plasma levels to oral risperidone[5]

- **OKEDI®** achieved similar mean active moiety plasma concentrations as oral risperidone at steady-state just **12 hours** after the first administration[5]

## Sustained and controlled release of OKEDI®, maintained during treatment[5]

- **OKEDI®** achieves steady-state following dose one[5]
- At steady-state, mean **average concentration** of the active moiety was **38.63 ng/mL** for the 100 mg dose[5]
- Mean **minimum concentration** of the active moiety was **21.22 ng/mL** for the 100 mg dose[5]

**Achieving therapeutic plasma levels similar to oral risperidone from Day 1, that are sustained throughout the 28-day dosing period[5]**

**Relieves patients from oral supplementation and loading doses[1,5]**

# Short and long-term efficacy and tolerability[2,4]

## PRISMA-3: SHORT-TERM STUDY

Efficacy and satefy of once-monthly OKEDI® in
**schizophrenia patients with an acute exacerbation**[2]

## STUDY DESIGN[2]

**Phase III, multicentre, randomised, double-blind, placebo-controlled clinical trial[2]**

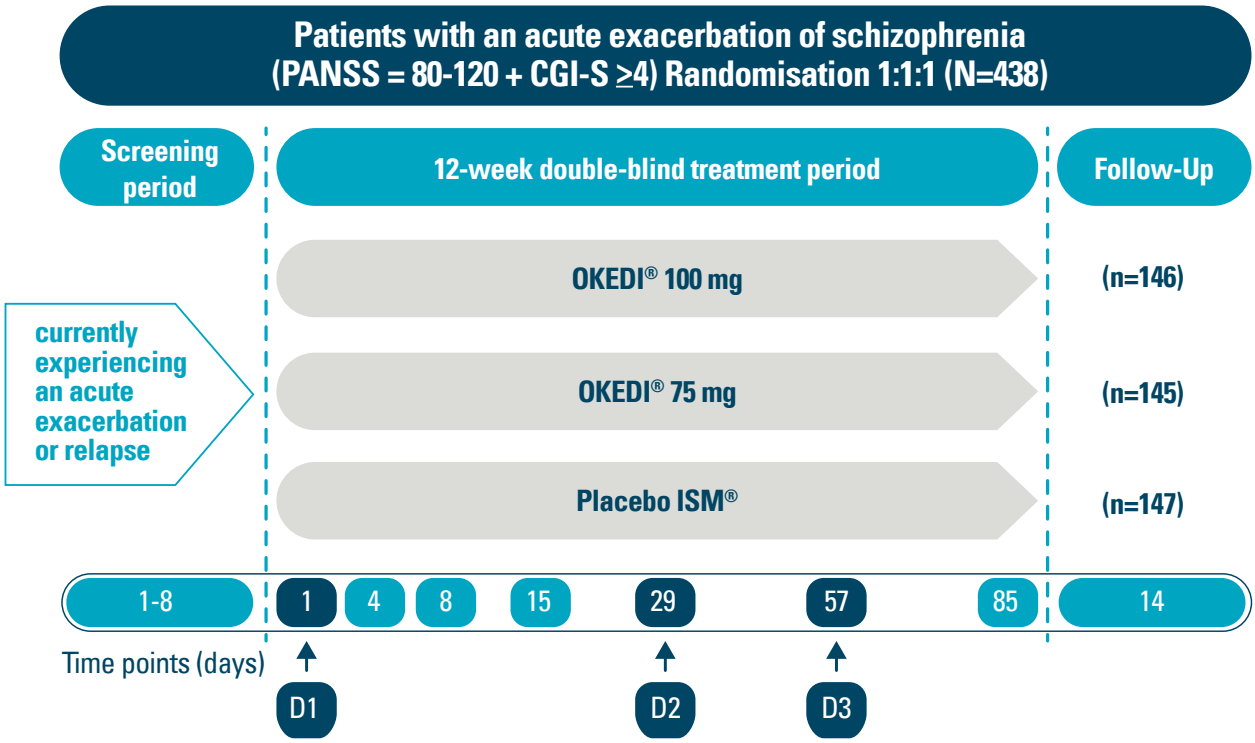


Diagram adapted from Correl CU, Litman RE, Filts Y, Llaudó J, Torres F, Martínez J. Efficacy and safety of once-monthly Risperidone ISM® in schizophrenic patients with an acute exacerbation. NJP Schizophr. 2020 Nov 25;6(1):37[2]

## PATIENTS[2]

**Currently experiencing an acute exacerbation or relapse**

- **PANSS total score 80-120**
  (with a score ≥4 points for ≥2 of the following positive symptom items: delusions, conceptual disorganisation, hallucinatory behaviour, and suspiciousness/persecution)
- **CGI-S of ≥4**

Other inclusion criteria:

- **Current diagnosis of schizophrenia** (according to the DSM-5 criteria)
- **18-65 years, BMI 18.5-40.0 kg/m² and previous clinical response to antipsychotic medication** other than clozapine

**PANSS:** Positive And Negative Syndrome Scale; **CGI-S:** Clinical Global Impression-Severity Scale; **D:** Dose; **DSM-5:** Diagnostic and Statistical Manual of Mental Disorders, 5th edition; **BMI:** Body Mass Index; **DB:** Double-blind.

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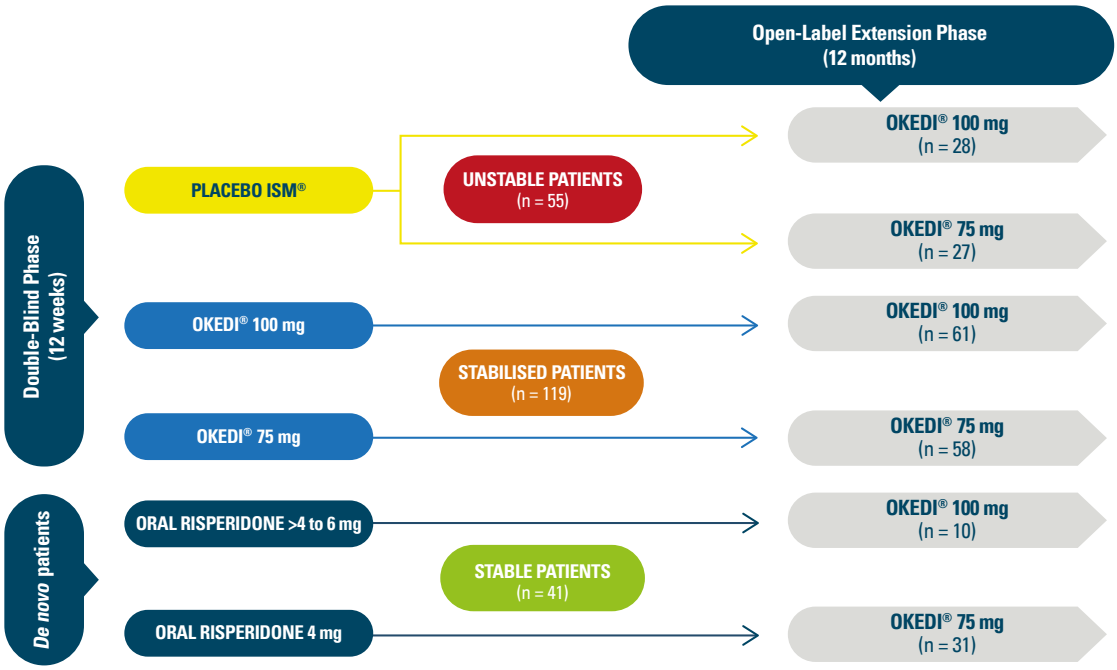
## PRISMA-3: LONG-TERM STUDY

# Long-term efficacy and safety

of once-monthly OKEDI® in the treatment of schizophrenia: Results from a **12-month** open-label extension study[4]

## STUDY DESIGN[4]

### 12-month open-label extension of the PRISMA-3 study[4]




## PATIENTS[4]

**Current diagnosis of schizophrenia** (DSM-5 criteria) & age ≥18 and ≤65

**3 Study groups**

**Unstable patients**
Completed the 12-week DB phase receiving placebo, were randomly assigned to OKEDI® 75 mg or 100 mg

**Stabilised patients**
Completed the 12-week DB phase receiving OKEDI®, continued receiving OKEDI® at the same dose

**Stable patients (*de novo*)**
Stable patients (*PANSS score <70, CGI-S ≤3 and without significant symptom exacerbation or hospitalisations due to relapses in the 3 months prior to screening*) receiving prior oral risperidone (4-6 mg/day) for 4 weeks, received OKEDI®:

- 4 mg oral risperidone → OKEDI® 75 mg
- >4 - 6 mg oral risperidone → OKEDI® 100 mg

# OKEDI® demonstrated efficacy in the short-term treatment of schizophrenia[2]

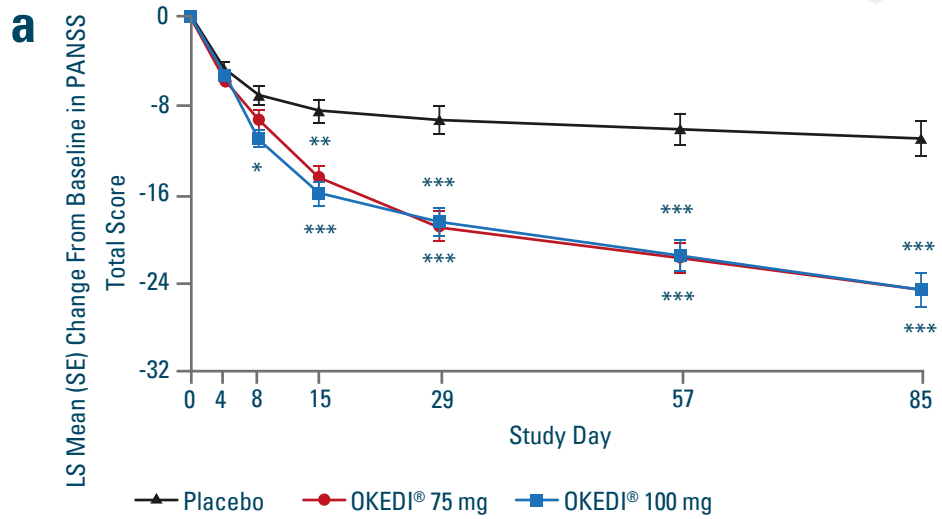
## PRIMARY EFFICACY VARIABLE

**PANSS total score**
mean change from baseline to Day 85[1]

**PANSS**

**-24.6 points** with **OKEDI® 75 mg**
(CI 95%: -27.5 to -21.6); **(p <0.0001)**

**-24.7 points** with **OKEDI® 100 mg**
(CI 95%: -27.7 to -21.6); **(p <0.0001)**




**Placebo-adjusted PANSS total score**
mean change from baseline to Day 85[2]

**-13.0 points** with **OKEDI® 75 mg**
(CI 95%, –17.3 to –8.8); **(p <0.0001)**

**-13.3 points** with **OKEDI® 100 mg**
(CI 95%, –17.6 to –8.9); **(p <0.0001)**

**Fig. LS mean change from baseline at each time point (mITT population). a** PANSS total score, where mean PANSS score at baseline for placebo= 96.4 (SD: 7.21), for OKEDI® 75 mg= 96.3 (SD: 8.47) and for OKEDI® 100 mg= 96.1 (SD: 8.42). The error bars represent SE and P values are for OKEDI® 75 mg and OKEDI® 100 mg dose group versus placebo (*p <0.01, **p < 0.001, ***p <0.0001).

## OKEDI® achieves sustained therapeutic plasma levels from DAY 1[1,2]...

### PANSS positive and negative subscale scores

OKEDI® 75 mg and 100 mg also **significantly improved patients' positive subscale score as early as day 8 and negative subscale score as early as day 15[2].** Positive subscale (75 mg, p <0.05; 100 mg, p <0.001), Negative subscale (both doses, p <0.05).

**CI:** Confidence Interval; **CGI-S:** Clinical Global Impression - Severity Scale; **mITT**: modified Intent-To-Treat; **LS:** Least Squares; **PANSS:** Positive And Negative Syndrome Scale; **SE:** Standard Error; **SD:** Standard Deviation.

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# KEY SECONDARY EFFICACY VARIABLE

## CGI-S score
mean change from baseline to Day 85[1]

**CGI-S**

**-1.3 points**
with both
**OKEDI® 75 mg and 100 mg**

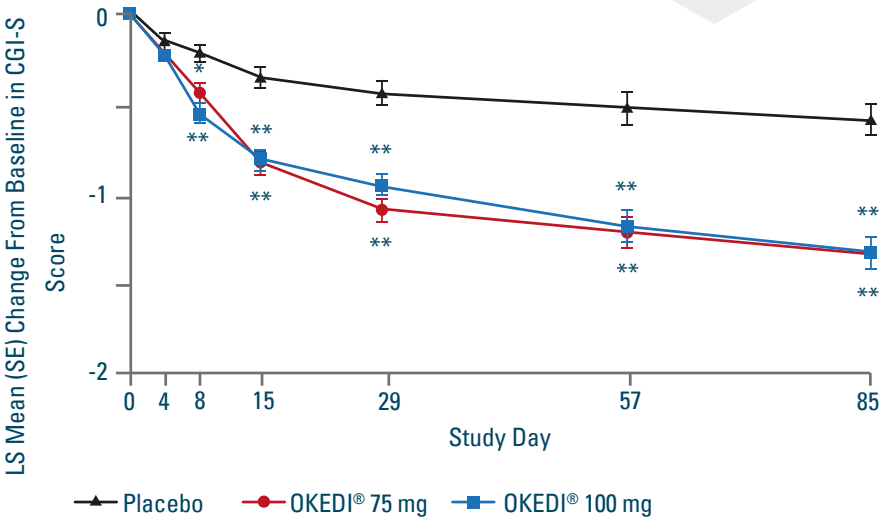
(CI 95%: -1.5 to -1.2);
**(p <0.0001)**

**Placebo-adjusted CGI-S score**
mean change from baseline to Day 85[2]

**-0.7 points**
with both
**OKEDI® 75 mg and 100 mg**

(CI 95%, -1.0 to -0.5);
**(p <0.0001)**

**b**




In **b** CGI-S Score, where mean CGI-S score at baseline for placebo= 4.9 (SD: 0.54), OKEDI® 75 mg= 4.9 (SD: 0.63) and OKEDI® 100 mg= 4.8 (SD: 0.53). The error bars represent SE and P values are for OKEDI® 75 mg and OKEDI® 100 mg dose group versus placebo (*p <0.01, **p <0.0001).

**...providing a significant# symptom reduction as early as DAY 8 compared to placebo, without the need for loading doses or oral risperidone supplementation in patients with schizophrenia following a relapse[1]**

#CGI-S: p <0.01 and p <0.0001 for the 75 and 100 mg doses respectively

## Overall response rate

For overall response rate at endpoint, the differences in proportions versus placebo were 39.2% (n=50/129; 95% CI: 27.5-49.2) for OKEDI® 75 mg and 33.8% (n=43/129; 95% CI: 22.0-43.8) for OKEDI® 100 mg (p <0.0001 for both groups, Mantel-Haenszel Test)

# OKEDI® demonstrated safety and tolerability in the short-term treatment

## SAFETY AND TOLERABILITY RESULTS

- Both doses of **OKEDI®** were generally well tolerated[2]
- The incidence of serious TEAEs (≤3.4%) and of TEAEs leading to study drug discontinuation (≤6.2%) were low and no significant differences between treatment groups were observed[2]
- The most frequently reported TEAEs were:[1]

| | |
|---|---|
| Blood prolactin increased | 11.7% |
| Hyperprolactinaemia | 7.2% |
| Akathisia | 5.5% |
| Headache | 4.8% |
| Somnolence | 4.1% |
| Weight increased | 3.8% |
| Injection site pain | 3.1% |
| Dizziness | 3.1% |

**TEAE:** Treatment-Emergent Adverse Event.

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# CONCLUSIONS

**OKEDI®** achieves **therapeutic levels from DAY 1** without the need for oral risperidone supplementation or loading doses, keeping these levels sustained throughout the full dosing period[1,5]

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**OKEDI®** provides a significant **improvement in symptoms and illness severity** as early as **day 8[2]**

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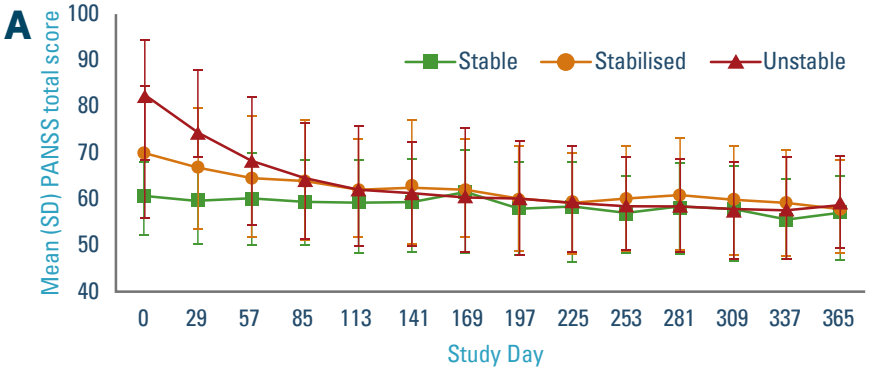
**OKEDI®** is an **effective and generally well tolerated therapeutic strategy for treating schizophrenia** in adults for whom tolerability and effectiveness have been established with oral risperidone[1]

# OKEDI® demonstrated efficacy in the long-term treatment of schizophrenia[4]

## In the 12-month Open-Label Extension, OKEDI® well tolerated for the long-term treatment of disease severity[4]

**PANSS total score**




At approximately 6 months (Day 169), the mean (SD) PANSS total scores in the unstable and stabilised patients were similar (60.6 [12.58] and 61.6 [13.78], respectively) to the score of stable patients at entry into the OLE study (60.3 [8.22])

**CGI-S**

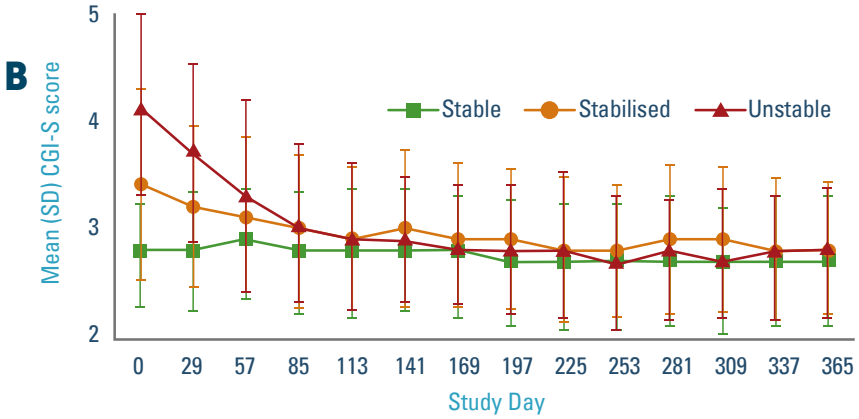



Fig. Mean (SD) PANSS total score (A) and CGI-S score (B) at each time point in Unstable, Stabilised and Stable patients treated with monthly OKEDI® (pooled 75 and 100 mg).

At approximately 4 months (Day 113), the mean CGI-S score in both unstable and stabilised patients reached mean (SD) values (2.9 [0.71] and 2.9 [0,67], respectively) similar to those shown at baseline by the stable patients prior to entering the OLE study (2.8 [0.52])

› **Unstable and stabilised patients reached a mean PANSS total score and a mean CGI-S score at months 6 and 4**, respectively, similar to those shown at baseline in stable patients[4]

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# proved to be effective, and generally schizophrenia in adults, regardless of the initial

## OKEDI® demonstrated a low overall relapse rate of

**10.7%**



[95% CI, 6.9% to 15.6%]
[23/215] in 12 months[4]

which demonstrates sustained relapse prevention over the long-term[4]

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Only **9 out of 215** patients required rehospitalisation[4]

**4.2%**



in 12 months[4]

**PANSS:** Positive And Negative Syndrome Scale; **SD:** Standard Deviation; **OLE:** Open-Label Extension; **CGI-S:** Clinical Global Impression-Severity Scale; **CI:** Confidence Interval.

# OKEDI® was generally well tolerated in treatment of schizophrenia[4]

Only **7 out of 215** patients discontinued treatment due to TEAEs related to **OKEDI®**[4]

**3.3%**

in 12 months[4]



## Summary of treatment-related TEAEs leading to study drug discontinuation and their overall incidence[4]

| | OKEDI® 75 mg (n = 116) | | OKEDI® 100 mg (n = 99) | | All OKEDI® (n = 215) | |
|---|---|---|---|---|---|---|
| | Overall incidence | Leading to discontinuation | Overall incidence | Leading to discontinuation | Overall incidence | Leading to discontinuation |
| **Akathisia** | 4 (3.4) | 0 | 4 (4.0) | 1 (1.0) | 8 (3.7) | 1 (0.5) |
| **Diabetes mellitus** | 1 (0.9) | 1 (0.9) | 0 | 0 | 1 (0.5) | 1 (0.5) |
| **Extrapyramidal disorder** | 1 (0.9) | 1 (0.9) | 0 | 0 | 1 (0.5) | 1 (0.5) |
| **Gynaecomastia** | 0 | 0 | 1 (1.0) | 1 (1.0) | 1 (0.5) | 1 (0.5) |
| **Hepatic steatosis** | 0 | 0 | 1 (1.0) | 1 (1.0) | 1 (0.5) | 1 (0.5)[a] |
| **Hepatocellular injury** | 0 | 0 | 1 (1.0) | 1 (1.0) | 1 (0.5) | 1 (0.5)[a] |
| **Libido decreased** | 3 (2.6) | 1 (0.9) | 0 | 0 | 3 (1.4) | 1 (0.5) |
| **Bodyweight increased** | 6 (5.2) | 1 (0.9) | 3 (3.0) | 0 | 9 (4.2) | 1 (0.5) |
| **Total** | 15 (12.9) | 4 (3.4) | 9 (9.1) | 3 (3.0) | 24 (11.2) | 7 (3.3) |

Data are presented as n (%). Description of TEAEs is coded using MedDRA version 22.1. [a]The same patient had 2 treatment-related TEAEs leading to discontinuation.

- 84 (39.1%) patients reported at least one treatment-related TEAE, with the majority being mild to moderate in severity[1]

# the long-term

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## OKEDI® was generally well tolerated over the long-term with a low incidence of TEAEs that are considered most bothersome for patients[4,6]

**Only 1** patient (0.5%) discontinued treatment with **OKEDI®** due to decreased libido (Overall incidence of 1.4%)[4]

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**Only 1** patient (0.5%) discontinued treatment with **OKEDI®** due to akathisia (Overall incidence of 3.7%)[4]

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**Only 1** patient (0.5%) discontinued treatment with **OKEDI®** due to extrapyramidal disorder (Overall incidence of 0.5%)[4]

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**Only 1** patient (0.5%) discontinued treatment with **OKEDI®** due to gynaecomastia (Overall incidence of 0.5%)[4]

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**Only 1** patient (0.5%) discontinued treatment with **OKEDI®** due to increased bodyweight (Overall incidence of 4.2%)[4]

**TEAE:** Treatment-Emergent Adverse Event.

# OKEDI® with innovative ISM® techno
# long-acting injectable antipsychotic

## INDICATED FOR THE TREATMENT OF SCHIZOPHRENIA IN ADULTS

for whom tolerability and effectiveness have been established with oral risperidone[1]

## OKEDI® posology[1]

Patients with history of **previous response to risperidone currently stabilised with oral antipsychotics**[1]

| Stabilised with oral risperidone | Stabilised with other oral antipsychotics |
|---|---|
| Direct switch to **OKEDI® 75 or 100 mg** | At least **6 days** on oral risperidone before administering **OKEDI® 75 or 100 mg** |



Patients **never treated before with oral risperidone**[1]

At least **14 days** on oral risperidone before administering **OKEDI® 75 or 100 mg**

# logy, is a 4-weekly from ROVI[1]

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## The **recommended doses** of **OKEDI®** are:[1]

**OKEDI® 75 mg**
every 4 weeks
when switching from
oral risperidone 3 mg/day

**OKEDI® 100 mg**
every 4 weeks
when switching from
oral risperidone 4 mg/day
or higher

**OKEDI® 75 mg and 100 mg powder and solvent for prolonged release suspension for intramuscular (IM) injection**
**Prescribing information**

**Please refer to Summary of Product Characteristics (SmPC) before prescribing.**

**Presentation:** Each pre-filled syringe contains 75 mg or 100 mg risperidone. **Indication:** OKEDI is indicated for the treatment of schizophrenia in adults for whom tolerability and effectiveness to risperidone have been established. **Posology and Method of Administration:** OKEDI should be administered by a qualified healthcare provider and ***initiated according to the patient's clinical context - see SmPC for detailed guidance.*** Administer OKEDI every 28 days by IM deltoid or gluteal injection. For full details on the preparation, reconstitution, and administration, see *'Instructions for healthcare professionals'* provided in the package leaflet. A maintenance dose of OKEDI 75 mg every 28 days is generally recommended. Some patients may benefit from OKEDI 100 mg every 28 days according to clinical response and tolerability. Neither a loading dose nor supplemental oral risperidone is recommended. **Elderly:** safety and efficacy of OKEDI for patients > 65 years have not been established. **Renal impairment: Mild** (creatinine clearance 60 to 89 mL/min) no dose adjustment required. **Moderate or severe** (creatinine clearance <60mL/min) not recommended. **Hepatic impairment:** use with caution. **CONTRAINDICATIONS:** Hypersensitivity to risperidone or any excipients. **SPECIAL WARNINGS & PRECAUTIONS:** Establish tolerability to oral risperidone prior to OKEDI. Rarely, anaphylactic reactions are reported in patients previously tolerating oral risperidone. If this occurs with OKEDI, discontinue treatment, initiate general supportive measures and monitor until resolved. Do not use in elderly patients with dementia. Caution in cerebrovascular disease, hypotension, cardiovascular disease (including family history of, or known QT prolongation), Parkinson's Disease, Lewy body dementia, seizures, and prolactin-dependent tumours. Monitoring of white blood cell count (WBC) may be needed. Discontinue OKEDI if a clinically significant decline in WBC occurs without other cause. If tardive dyskinesia occurs, consider discontinuation of all antipsychotics. Caution required in patients receiving concomitant psychostimulants (e.g., methylphenidate) and risperidone. Gradual withdrawal of psychostimulant recommended. Discontinue OKEDI if neuroleptic malignant syndrome occurs. Discontinue OKEDI if Stevens-Johnson syndrome/toxic epidermal necrolysis occurs. Weight gain is common. Monitor patients with, or at risk, of diabetes. Patients with prolonged priapism should seek urgent medical care. Body temperature dysregulation may occur. An antiemetic effect may mask signs and symptoms of other conditions including overdoses. Identify risk factors for venous thromboembolism and take preventative measures. Intraoperative floppy iris syndrome may increase cataract surgery complications. **Interactions with other medicinal products:** No interaction studies have been performed with OKEDI. See SmPC for extensive interaction data based on oral risperidone studies. **Pregnancy and breast feeding:** Should not be used during pregnancy unless clearly necessary. A risk to the breastfed child cannot be excluded. **Undesirable effects:** The most frequent adverse drug reactions reported in an OKEDI phase 3 trial were blood prolactin increased (11.7%), hyperprolactinaemia (7.2%), akathisia (5.5%), headache (4.8%), somnolence (4.1%), weight increased (3.8%), injection site pain (3.1%) and dizziness (3.1%). **Refer to the SmPC for other adverse reactions reported for risperidone from clinical trials and post marketing experience with risperidone medicinal products.**

**Legal Category:** Prescription Only Medicine (POM).

**Presentation and Basic NHS cost:** OKEDI 75 mg pack containing one pre-filled syringe - £222.64 OKEDI 100 mg pack containing one pre-filled syringe - £285.52.

**Marketing Authorisation (MA) Numbers:** PLGB 15406/0018 (75 mg), PLGB15406/0019 (100 mg). **MA Holder:** Laboratorios Farmacéuticos Rovi, S.A., Julián Camarillo, 35, 28037 Madrid, Spain. **Date of Preparation:** November 2023.

UK-OKE-23-11/0002

**Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/ or search for MHRA Yellowcard in the Google Play or Apple App Store. Adverse events should also be reported to uk-pharmacovigilance@rovi.com or by telephone +44 (0) 203 642 0677**

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**OKEDI® is indicated for the treatment of schizophrenia in adults for whom tolerability and effectiveness have been established with oral risperidone[1]**

# A DISTINCTIVE PATH FOR YOUR PATIENTS FROM DAY 1[1,2]

**No need for oral supplementation or loading doses which may improve the therapeutic alliance[1,3]**

- Achieving therapeutic plasma levels similar to oral risperidone from Day 1, that are sustained throughout the 28-day dosing period[5]
- No requirement for oral supplementation or loading doses[1]
- Generally well tolerated in a 12-month open-label extension study[4]
- May help improve adherence, allowing a focus on patients' psychosocial recovery[4,7]

Adverse events should be reported.
Reporting forms and information can be found at
**www.mhra.gov.uk/yellowcard**
Adverse events should also be reported to Rovi Biotech Limited UK
on **+44 (0) 203 642 06 77** or **uk-pharmacovigilance@rovi.com**


**References:**

**1.** Okedi® SmPC.

**2.** Correll CU, Litman RE, Filts Y, Llaudó J, Naber D, Torres F, Martínez J. Efficacy and safety of once-monthly Risperidone ISM® in schizophrenic patients with an acute exacerbation. NPJ Schizophr. 2020 Nov 25;6(1):37.

**3.** Walling DP, Hassman HA, Anta L, Ochoa L, Ayani I, Martinez J, Gutierro I. The Steady-State Comparative Bioavailability of Intramuscular Risperidone ISM and Oral Risperidone: An Open-Label, One-Sequence Study Drug Des Devel Ther. 2021;15:4371-4382 [published correction appears in Drug Des Devel Ther. 2022 Jun 13;16:1791-1792].

**4.** Filts Y, Litman RE, Martínez J, Anta L, Naber D, Correll CU. Long-term efficacy and safety of once-monthly Risperidone ISM® in the treatment of schizophrenia: Results from a 12-month open-label extension study [published correction appears in Schizophr Res. 2022 Aug;246:258-259]. Schizophr Res. 2022;239:83-91.

**5.** Walling DP, Hassman HA, Anta L, Ochoa L, Ayani I, Martinez J, Gutierro I. The Steady-State Comparative Bioavailability of Intramuscular Risperidone ISM and Oral Risperidone: An Open-Label, One-Sequence Study Drug Des Devel Ther. 2021;15:4371-4382 [published correction appears in Drug Des Devel Ther. 2022 Jun 13;16:1791-1792].

**6.** Llorca PM, Lançon C, Hartry A, et al. Assessing the burden of treatment-emergent adverse events associated with atypical antipsychotic medications. BMC Psychiatry 2017 Feb 13;17(1).67.

**7.** Yildiz M. Psychosocial Rehabilitation Interventions in the Treatment of Schizophrenia and Bipolar Disorder. Noro Psikiyatr Ars. 2021 Sep 20;58(Suppl 1):S77-S82.


ROVI

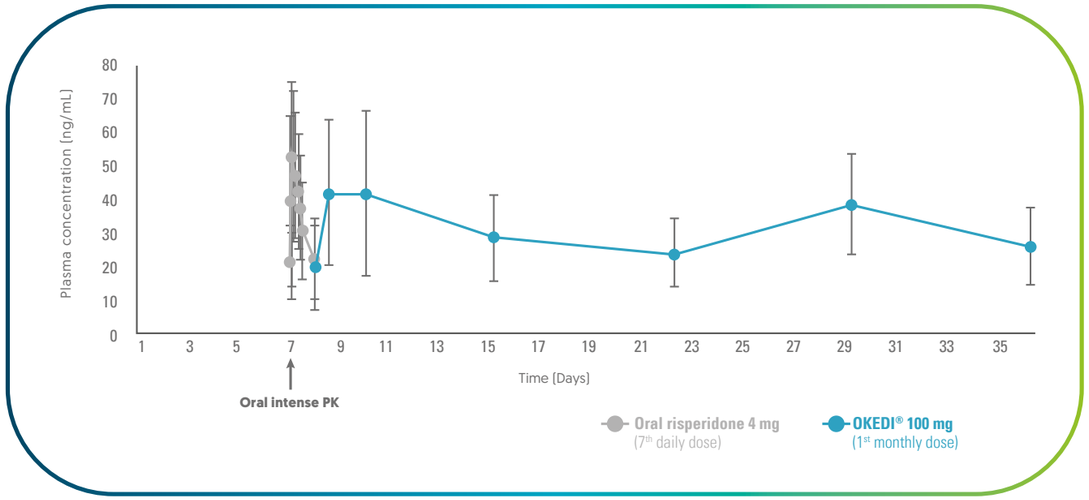
## OKEDI®, with innovative ISM® technology, is a convenient 4-weekly long-acting injectable antipsychotic from ROVI

# INDICATED FOR THE TREATMENT OF SCHIZOPHRENIA IN ADULTS

for whom tolerability and effectiveness have been established with oral risperidone[1]

**Effective and generally well tolerated 4-weekly risperidone LAI developed to offer a convenient path for your patients from Day 1[1,2]**

**OKEDI®** rapidly achieves **therapeutic plasma levels on Day 1**, which are **sustained throughout the dosing period** without the need for loading doses or oral supplementation.[1,5]




Mean (±SD) plasma concentrations versus time profiles for risperidone active moiety during oral risperidone 4 mg treatment (7th dose) and after switching to OKEDI® 100 mg (PK population). Notes: Once daily oral risperidone 4 mg was administered for 7 days. An intense oral pharmacokinetic (PK) analysis was conducted at study Day 7 (last day of the oral risperidone treatment) including samples at pre-dose (within 0.5 hours relative to the dose time), 1, 2, 3, 4, 6, 8, and 12 hours, post-dose (grey line). Twenty-four hours after the last oral risperidone dose (study Day 8), a single intramuscular dose of OKEDI® 100 mg was administered and PK samples were obtained at pre-dose and 12 hours post-dose, as well as at Days 10, 15, 22, 29, and 36 (blue line).[5]

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**Immediate release of OKEDI®, achieving similar plasma levels to oral risperidone[5]**

- **OKEDI®** **achieved similar mean active moiety plasma concentrations** as oral risperidone at steady-state just **12 hours** after the first administration[5]

**Sustained and controlled release of OKEDI®, maintained during treatment[5]**

- **OKEDI®** achieves steady-state following dose one[5]
- At steady-state, mean **average concentration** of the active moiety was **38.63 ng/mL** for the 100 mg dose[5]
- Mean **minimum concentration** of the active moiety was **21.22 ng/mL** for the 100 mg dose[5]

**Achieving therapeutic plasma levels similar to oral risperidone from Day 1, that are sustained throughout the 28-day dosing period[5]**

**Relieves patients from oral supplementation and loading doses[1,5]**

**LAI:** Long-Acting Injectable; **SD**: Standard Deviation.

# Short and long-term efficacy and tolerability[2,4]

Okedi®
Risperidone prolonged-release suspension for injection 75 mg, 100 mg

## PRISMA-3: SHORT-TERM STUDY

Efficacy and satefy of once-monthly OKEDI® in
**schizophrenia patients with an acute exacerbation**[2]

### STUDY DESIGN[2]

**Phase III, multicentre, randomised, double-blind, placebo-controlled clinical trial[2]**

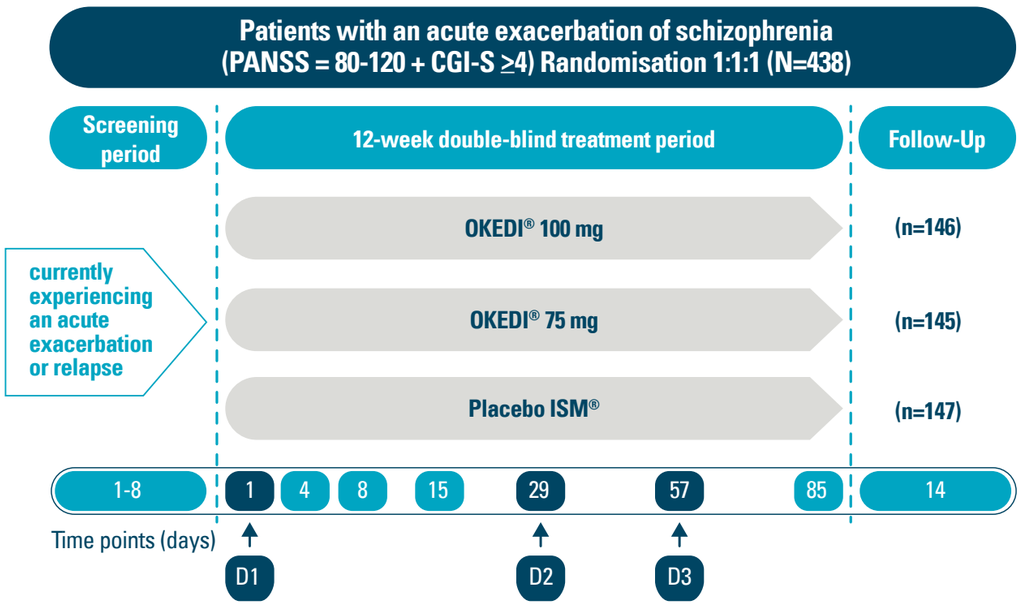



Diagram adapted from Correl CU, Litman RE, Filts Y, Llaudó J, Torres F, Martínez J. Efficacy and safety of once-monthly Risperidone ISM® in schizophrenic patients with an acute exacerbation. NJP Schizophr. 2020 Nov 25;6(1):37[2]

### PATIENTS[2]

**Currently experiencing an acute exacerbation or relapse**

- **PANSS total score 80-120**
  (with a score ≥4 points for ≥2 of the following positive symptom items: delusions, conceptual disorganisation, hallucinatory behaviour, and suspiciousness/persecution)
- **CGI-S of ≥4**

Other inclusion criteria:

- **Current diagnosis of schizophrenia** (according to the DSM-5 criteria)
- **18-65 years, BMI 18.5-40.0 kg/m² and previous clinical response to antipsychotic medication** other than clozapine

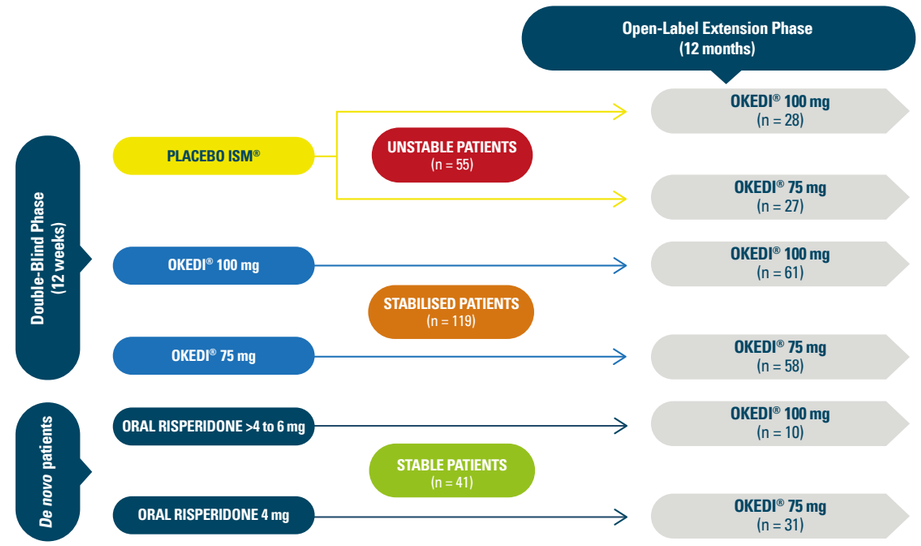
**PANSS:** Positive And Negative Syndrome Scale; **CGI-S:** Clinical Global Impression-Severity Scale; **D:** Dose; **DSM-5:** Diagnostic and Statistical Manual of Mental Disorders, 5th edition; **BMI:** Body Mass Index; **DB:** Double-blind.

## PRISMA-3: LONG-TERM STUDY

**Long-term efficacy and safety**
of once-monthly OKEDI® in the treatment of schizophrenia:
Results from a **12-month** open-label extension study[4]

### STUDY DESIGN[4]

**12-month open-label extension of the PRISMA-3 study[4]**




### PATIENTS[4]

**Current diagnosis of schizophrenia** (DSM-5 criteria) & age ≥18 and ≤65
**3 Study groups**

**Unstable patients**
Completed the 12-week DB phase receiving placebo, were randomly assigned to OKEDI® 75 mg or 100 mg

**Stabilised patients**
Completed the 12-week DB phase receiving OKEDI®, continued receiving OKEDI® at the same dose

**Stable patients (*de novo*)**
Stable patients (*PANSS score <70, CGI-S ≤3 and without significant symptom exacerbation or hospitalisations due to relapses in the 3 months prior to screening*) receiving prior oral risperidone (4-6 mg/day) for 4 weeks, received OKEDI®:

- 4 mg oral risperidone → OKEDI® 75 mg
- >4 - 6 mg oral risperidone → OKEDI® 100 mg

# OKEDI® demonstrated efficacy in the short-term treatment of schizophrenia[2]

Okedi®
Risperidone prolonged-release suspension for injection 75 mg, 100 mg

## PRIMARY EFFICACY VARIABLE

**PANSS total score**
mean change from baseline to Day 85[1]

**PANSS**

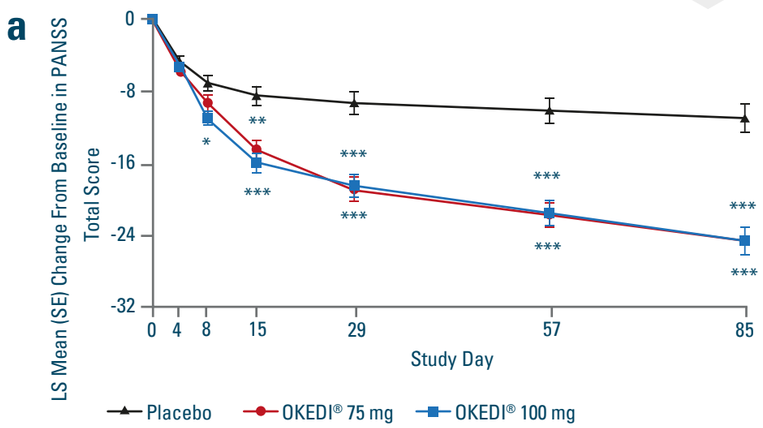
**-24.6 points** with **OKEDI® 75 mg**
(CI 95%: -27.5 to -21.6); **(p <0.0001)**

**-24.7 points** with **OKEDI® 100 mg**
(CI 95%: -27.7 to -21.6); **(p <0.0001)**

**Placebo-adjusted PANSS total score**
mean change from baseline to Day 85[2]

**-13.0 points** with **OKEDI® 75 mg**
(CI 95%, −17.3 to −8.8); **(p <0.0001)**

**-13.3 points** with **OKEDI® 100 mg**
(CI 95%, −17.6 to −8.9); **(p <0.0001)**




## KEY SECONDARY EFFICACY VARIABLE

**CGI-S score**
mean change from baseline to Day 85[1]

**CGI-S**

**-1.3 points** with both **OKEDI® 75 mg and 100 mg**
(CI 95%: -1.5 to -1.2); **(p <0.0001)**

**Placebo-adjusted CGI-S score**
mean change from baseline to Day 85[2]

**-0.7 points** with both **OKEDI® 75 mg and 100 mg**
(CI 95%, -1.0 to -0.5); **(p <0.0001)**

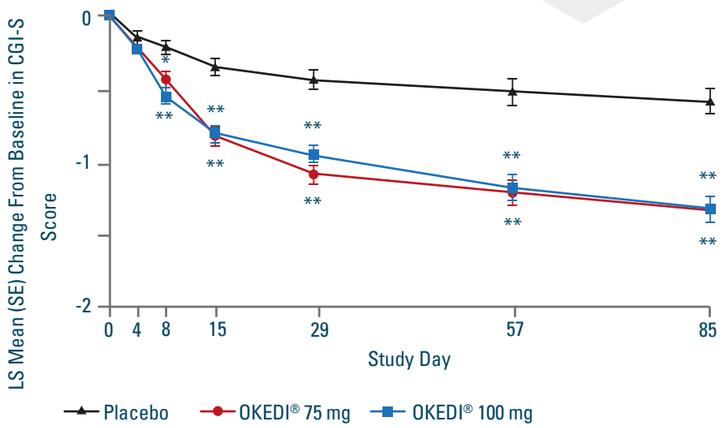



**Fig. LS mean change from baseline at each time point (mITT population). a** PANSS total score, where mean PANSS score at baseline for placebo= 96.4 (SD: 7.21), for OKEDI® 75 mg= 96.3 (SD: 8.47) and for OKEDI® 100 mg= 96.1 (SD: 8.42). The error bars represent SE and P values are for OKEDI® 75 mg and OKEDI® 100 mg dose group versus placebo (*p <0.01, **p < 0.001, ***p <0.0001).

In **b** CGI-S Score, where mean CGI-S score at baseline for placebo= 4.9 (SD: 0.54), OKEDI® 75 mg= 4.9 (SD: 0.63) and OKEDI® 100 mg= 4.8 (SD: 0.53). The error bars represent SE and P values are for OKEDI® 75 mg and OKEDI® 100 mg dose group versus placebo (*p <0.01, **p <0.0001).

**OKEDI® achieves sustained therapeutic plasma levels from DAY 1[1,2]...**

**...providing a significant# symptom reduction as early as DAY 8 compared to placebo, without the need for loading doses or oral risperidone supplementation in patients with schizophrenia following a relapse[1]**
#CGI-S: p <0.01 and p <0.0001 for the 75 and 100 mg doses respectively

### PANSS positive and negative subscale scores

OKEDI® 75 mg and 100 mg also **significantly improved patients' positive subscale score as early as day 8 and negative subscale score as early as day 15[2].** Positive subscale (75 mg, p <0.05; 100 mg, p <0.001), Negative subscale (both doses, p <0.05).

### Overall response rate

For overall response rate at endpoint, the differences in proportions versus placebo were 39.2% (n=50/129; 95% CI: 27.5-49.2) for OKEDI® 75 mg and 33.8% (n=43/129; 95% CI: 22.0-43.8) for OKEDI® 100 mg (p <0.0001 for both groups, Mantel-Haenszel Test)

**CI:** Confidence Interval; **CGI-S:** Clinical Global Impression - Severity Scale; **mITT**: modified Intent-To-Treat; **LS:** Least Squares; **PANSS:** Positive And Negative Syndrome Scale; **SE:** Standard Error; **SD:** Standard Deviation.

# OKEDI® demonstrated safety and tolerability in the short-term treatment of schizophrenia[2]

Okedi®
Risperidone prolonged-release suspension for injection 75 mg, 100 mg

## SAFETY AND TOLERABILITY RESULTS

- Both doses of **OKEDI®** were generally well tolerated[2]
- The incidence of serious TEAEs (≤3.4%) and of TEAEs leading to study drug discontinuation (≤6.2%) were low and no significant differences between treatment groups were observed[2]
- The most frequently reported TEAEs were:[1]

| | |
|---|---|
| Blood prolactin increased | 11.7% |
| Hyperprolactinaemia | 7.2% |
| Akathisia | 5.5% |
| Headache | 4.8% |
| Somnolence | 4.1% |
| Weight increased | 3.8% |
| Injection site pain | 3.1% |
| Dizziness | 3.1% |

## CONCLUSIONS

**OKEDI®** achieves **therapeutic levels from DAY 1** without the need for oral risperidone supplementation or loading doses, keeping these levels sustained throughout the full dosing period[1,5]

**OKEDI®** provides a significant **improvement in symptoms and illness severity** as early as **day 8[2]**

**OKEDI®** is an **effective and generally well tolerated therapeutic strategy for treating schizophrenia** in adults for whom tolerability and effectiveness have been established with oral risperidone[1]

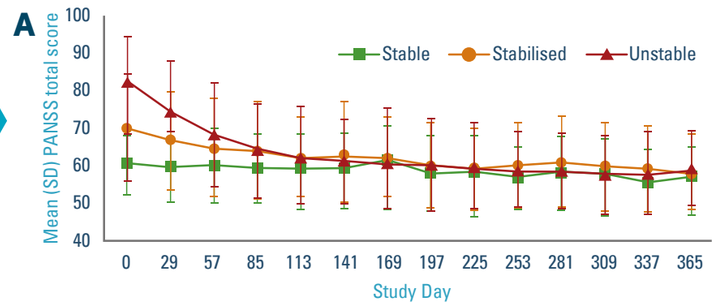
**TEAE:** Treatment-Emergent Adverse Event.

# OKEDI® demonstrated efficacy in the long-term treatment of schizophrenia[4]

Okedi®
Risperidone prolonged-release suspension for injection 75 mg, 100 mg

## In the 12-month Open-Label Extension, OKEDI® proved to be effective, and generally well tolerated for the long-term treatment of schizophrenia in adults, regardless of the initial disease severity[4]

**PANSS total score**




At approximately 6 months (Day 169), the mean (SD) PANSS total scores in the unstable and stabilised patients were similar (60.6 [12.58] and 61.6 [13.78], respectively) to the score of stable patients at entry into the OLE study (60.3 [8.22])

**CGI-S**

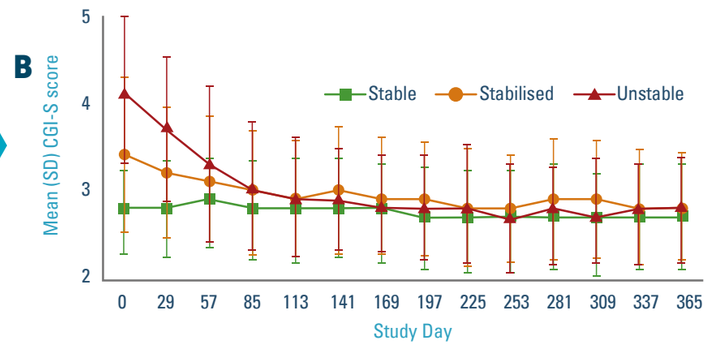



Fig. Mean (SD) PANSS total score (A) and CGI-S score (B) at each time point in Unstable, Stabilised and Stable patients treated with monthly OKEDI® (pooled 75 and 100 mg).

At approximately 4 months (Day 113), the mean CGI-S score in both unstable and stabilised patients reached mean (SD) values (2.9 [0.71] and 2.9 [0,67], respectively) similar to those shown at baseline by the stable patients prior to entering the OLE study (2.8 [0.52])

› **Unstable and stabilised patients reached a mean PANSS total score and a mean CGI-S score at months 6 and 4**, respectively, similar to those shown at baseline in stable patients[4]

**OKEDI® demonstrated a low overall relapse rate of**

**10.7%**

(95% CI, 6.9% to 15.6%)
[23/215] in 12 months[4]

which demonstrates sustained relapse prevention over the long-term[4]

Only **9 out of 215** patients required rehospitalisation[4]

**4.2%**

in 12 months[4]

**PANSS:** Positive And Negative Syndrome Scale; **SD:** Standard Deviation; **OLE:** Open-Label Extension; **CGI-S:** Clinical Global Impression-Severity Scale; **CI:** Confidence Interval.

# OKEDI® was generally well tolerated in the long-term treatment of schizophrenia[4]

Okedi®
Risperidone prolonged-release suspension for injection 75 mg, 100 mg

Only **7 out of 215** patients discontinued treatment due to TEAEs related to **OKEDI®**[4]

**3.3%**
in 12 months[4]

**Summary of treatment-related TEAEs leading to study drug discontinuation and their overall incidence[4]**

| | OKEDI® 75 mg (n = 116) | | OKEDI® 100 mg (n = 99) | | All OKEDI® (n = 215) | |
|---|---|---|---|---|---|---|
| | Overall incidence | Leading to discontinuation | Overall incidence | Leading to discontinuation | Overall incidence | Leading to discontinuation |
| **Akathisia** | 4 (3.4) | 0 | 4 (4.0) | 1 (1.0) | 8 (3.7) | 1 (0.5) |
| **Diabetes mellitus** | 1 (0.9) | 1 (0.9) | 0 | 0 | 1 (0.5) | 1 (0.5) |
| **Extrapyramidal disorder** | 1 (0.9) | 1 (0.9) | 0 | 0 | 1 (0.5) | 1 (0.5) |
| **Gynaecomastia** | 0 | 0 | 1 (1.0) | 1 (1.0) | 1 (0.5) | 1 (0.5) |
| **Hepatic steatosis** | 0 | 0 | 1 (1.0) | 1 (1.0) | 1 (0.5) | 1 (0.5)[a] |
| **Hepatocellular injury** | 0 | 0 | 1 (1.0) | 1 (1.0) | 1 (0.5) | 1 (0.5)[a] |
| **Libido decreased** | 3 (2.6) | 1 (0.9) | 0 | 0 | 3 (1.4) | 1 (0.5) |
| **Bodyweight increased** | 6 (5.2) | 1 (0.9) | 3 (3.0) | 0 | 9 (4.2) | 1 (0.5) |
| **Total** | 15 (12.9) | 4 (3.4) | 9 (9.1) | 3 (3.0) | 24 (11.2) | 7 (3.3) |

Data are presented as n (%). Description of TEAEs is coded using MedDRA version 22.1. [a]The same patient had 2 treatment-related TEAEs leading to discontinuation.

› 84 (39.1%) patients reported at least one treatment-related TEAE, with the majority being mild to moderate in severity[1]

## OKEDI® was generally well tolerated over the long-term with a low incidence of TEAEs that are considered most bothersome for patients[4,6]

**Only 1** patient (0.5%) discontinued treatment with **OKEDI®** due to decreased libido (Overall incidence of 1.4%)[4]

**Only 1** patient (0.5%) discontinued treatment with **OKEDI®** due to akathisia (Overall incidence of 3.7%)[4]

**Only 1** patient (0.5%) discontinued treatment with **OKEDI®** due to extrapyramidal disorder (Overall incidence of 0.5%)[4]

**Only 1** patient (0.5%) discontinued treatment with **OKEDI®** due to gynaecomastia (Overall incidence of 0.5%)[4]

**Only 1** patient (0.5%) discontinued treatment with **OKEDI®** due to increased bodyweight (Overall incidence of 4.2%)[4]

**TEAE:** Treatment-Emergent Adverse Event.

# OKEDI® with innovative ISM® techno logy, is a 4-weekly long-acting injectable antipsychotic from ROVI[1]

Okedi®
Risperidone prolonged-release suspension for injection 75 mg, 100 mg

## INDICATED FOR THE TREATMENT OF SCHIZOPHRENIA IN ADULTS

for whom tolerability and effectiveness have been established with oral risperidone[1]

## OKEDI® posology[1]

Patients with history of **previous response to risperidone currently stabilised with oral antipsychotics[1]**

| Stabilised with oral risperidone | Stabilised with other oral antipsychotics |
|---|---|
| Direct switch to **OKEDI® 75 or 100 mg** | At least **6 days** on oral risperidone before administering **OKEDI® 75 or 100 mg** |

Patients **never treated before with oral risperidone[1]**

At least **14 days** on oral risperidone before administering **OKEDI® 75 or 100 mg**

The **recommended doses** of **OKEDI®** are:[1]

**OKEDI® 75 mg** every 4 weeks when switching from oral risperidone 3 mg/day

**OKEDI® 100 mg** every 4 weeks when switching from oral risperidone 4 mg/day or higher

**OKEDI® 75 mg and 100 mg powder and solvent for prolonged release suspension for intramuscular (IM) injection**
**Prescribing information**

**Please refer to Summary of Product Characteristics (SmPC) before prescribing.**

**Presentation:** Each pre-filled syringe contains 75 mg or 100 mg risperidone. **Indication:** OKEDI is indicated for the treatment of schizophrenia in adults for whom tolerability and effectiveness to risperidone have been established. **Posology and Method of Administration:** OKEDI should be administered by a qualified healthcare provider and ***initiated according to the patient's clinical context - see SmPC for detailed guidance.*** Administer OKEDI every 28 days by IM deltoid or gluteal injection. For full details on the preparation, reconstitution, and administration, see *'Instructions for healthcare professionals'* provided in the package leaflet. A maintenance dose of OKEDI 75 mg every 28 days is generally recommended. Some patients may benefit from OKEDI 100 mg every 28 days according to clinical response and tolerability. Neither a loading dose nor supplemental oral risperidone is recommended. **Elderly:** safety and efficacy of OKEDI for patients > 65 years have not been established. **Renal impairment: Mild** (creatinine clearance 60 to 89 mL/min) no dose adjustment required. **Moderate or severe** (creatinine clearance <60mL/min) not recommended. **Hepatic impairment:** use with caution. **CONTRAINDICATIONS:** Hypersensitivity to risperidone or any excipients. **SPECIAL WARNINGS & PRECAUTIONS:** Establish tolerability to oral risperidone prior to OKEDI. Rarely, anaphylactic reactions are reported in patients previously tolerating oral risperidone. If this occurs with OKEDI, discontinue treatment, initiate general supportive measures and monitor until resolved. Do not use in elderly patients with dementia. Caution in cerebrovascular disease, hypotension, cardiovascular disease (including family history of, or known QT prolongation), Parkinson's Disease, Lewy body dementia, seizures, and prolactin-dependent tumours. Monitoring of white blood cell count (WBC) may be needed. Discontinue OKEDI if a clinically significant decline in WBC occurs without other cause. If tardive dyskinesia occurs, consider discontinuation of all antipsychotics. Caution required in patients receiving concomitant psychostimulants (e.g., methylphenidate) and risperidone. Gradual withdrawal of psychostimulant recommended. Discontinue OKEDI if neuroleptic malignant syndrome occurs. Discontinue OKEDI if Stevens-Johnson syndrome/toxic epidermal necrolysis occurs. Weight gain is common. Monitor patients with, or at risk, of diabetes. Patients with prolonged priapism should seek urgent medical care. Body temperature dysregulation may occur. An antiemetic effect may mask signs and symptoms of other conditions including overdoses. Identify risk factors for venous thromboembolism and take preventative measures. Intraoperative floppy iris syndrome may increase cataract surgery complications. **Interactions with other medicinal products:** No interaction studies have been performed with OKEDI. See SmPC for extensive interaction data based on oral risperidone studies. **Pregnancy and breast feeding:** Should not be used during pregnancy unless clearly necessary. A risk to the breastfed child cannot be excluded. **Undesirable effects:** The most frequent adverse drug reactions reported in an OKEDI phase 3 trial were blood prolactin increased (11.7%), hyperprolactinaemia (7.2%), akathisia (5.5%), headache (4.8%), somnolence (4.1%), weight increased (3.8%), injection site pain (3.1%) and dizziness (3.1%). **Refer to the SmPC for other adverse reactions reported for risperidone from clinical trials and post marketing experience with risperidone medicinal products.**

**Legal Category:** Prescription Only Medicine (POM).

**Presentation and Basic NHS cost:** OKEDI 75 mg pack containing one pre-filled syringe - £222.64 OKEDI 100 mg pack containing one pre-filled syringe - £285.52.

**Marketing Authorisation (MA) Numbers:** PLGB 15406/0018 (75 mg), PLGB15406/0019 (100 mg). **MA Holder:** Laboratorios Farmacéuticos Rovi, S.A., Julián Camarillo, 35, 28037 Madrid, Spain. **Date of Preparation:** November 2023.

UK-OKE-23-11/0002

**Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/ or search for MHRA Yellowcard in the Google Play or Apple App Store.**
**Adverse events should also be reported to uk-pharmacovigilance@rovi.com or by telephone +44 (0) 203 642 0677**