

EDA Assessment Report for human medicinal product

(Scientific Discussion)

Miroxnoric 2.5 mg, 5 mg, 10 mg and 15 mg Film Coated Tablet

(Mirogabalin “As Besylate”)

Date: September 2026

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I. Introduction

Based on the review of the quality, safety and efficacy data, the Egyptian Drug Authority have granted marketing authorization for “Miroxnoric 2.5, 5, 10 and 15 mg” from P&C Labs (Pellets & CR Products)

The product is indicated for the treatment of peripheral neuropathic pain, diabetic peripheral neuropathic pain, and post-herpetic neuralgia.

II. Quality Aspect

Drug Substance

- An APIMF (Applicant/ restricted part) has been submitted for evaluation.
- The drug substance off-white to white colour powder, soluble in methanol and dimethyl sulfoxide, insoluble in Cylohexane. Mirogabalin besylate has three chiral centers. The active form is R-isomer. Mirogabalin besylate exhibits polymorphism, the crystalline form resulting from the manufacturing process adopted by the supplier is form I.
- The synthesis of drug substance includes five stages with the formation of four intermediates. All starting materials, reagents, solvents are well controlled.
- The drug substance is elucidated via mass spectrometry (MS), ^1H and ^{13}C nuclear magnetic resonance (NMR) spectroscopy, infrared spectroscopy (IR) and elemental analysis. Moreover, the crystalline form of Mirogabalin besylate has been confirmed by X-ray powder diffraction (XRD) and Thermal Gravimetric Analysis (TGA).
- The drug substance specifications include description, solubility, identification (IR), identification (HPLC), water content (KF), loss on drying, residue on ignition, heavy metals, Benzene sulfonic acid content (potentiometry), S-isomer content (HPLC), dimer content (HPLC), related substances (HPLC), residual solvents (GC), Nickel content (ICP-MS), X-ray diffraction and particle size distribution.
- Analytical methods were adequately described and validated

- The supplier provided batch analysis results of 3 drug substance batches demonstrating compliance with the current drug substance specification
- The API is packed in double lined low-density food grade polyethylene bag (transparent inner and black outer) tie with plastic fastener and followed by HDPE drums.
- Stability of API is submitted in accelerated ($40^{\circ}\text{C} \pm 2^{\circ}\text{C} / 75\% \pm 5\% \text{ RH}$) and long-term storage conditions ($25^{\circ}\text{C} \pm 2^{\circ}\text{C} / 60\% \pm 5\% \text{ RH}$) and conclude the conformity of specifications during the shelf life and storage conditions. The retest period of the API is 24 months when stored below 25°C in the proposed container

Medicinal Product

• Product Description

- For 2.5mg: Pale to deep green biconvex round non-scored film coated tablets with white to off white core.
- For 5mg: Faint red to dark brick red Round biconvex non scored film coated tablet with white to off white Core
- For 10mg: Pale to deep yellow Round biconvex non scored film coated tablet with white to off white Core
- For 15mg: White to off white Round biconvex non scored film coated tablet with white to off white Core
- The product is packed in carton box contain triplex (OPA/ AL/ PVC /AL) blister
- The excipients are D-Mannitol, Microcrystalline Cellulose pH 102, Starch 1500, Povidone K30, Crospovidone, Citric acid monohydrate, Magnesium Aluminum Silicate, Magnesium Stearate, Purified Water, Hypromellose (HPMC E5), Macrogol (PEG 600), Purified Talc, Titanium dioxide (C.I: 77891).
**For 2.5mg: Quinoline yellow (C.I: 47005) and Brilliant blue (C.I: 42090)
**For 5mg: Iron Oxide red (C.I: 77491)
**For 10 mg: Iron Oxide yellow (C.I: 77492)

• Pharmaceutical development,

- The development of the product has been described; the choice of excipients is justified and their functions explained. It was aimed to develop a product equivalent to the reference products of Mirogabalin besylate.
- Overall, the choices of the packaging, manufacturing process, compatibility, overage physicochemical properties and microbiological attributes are justified.

- **Manufacturing process**

- The manufacturing process consists of sieving, granulation, drying, sieving, milling, mixing, lubrication, compression, coating and blistering.
- The applicant submitted the process validation protocol of the manufacturing process in line with relevant guidelines and committed to provide the process validation report for the first three production batches.

- **Control of excipients**

- All excipients comply with B.P and USP except for Quinoline yellow and Brilliant blue which comply with in-house specifications.

- **Control of Drug Product**

- Product specifications include Description, colour of core, Disintegration, Mass Uniformity test, Water content (KF), Identification (HPLC & UV), Assay (HPLC), Dissolution, Uniformity of dosage units, Related Substances (HPLC) and Microbiological tests.
- Analytical methods were revised and found to be suitable for the required testing.
- Batch Analysis from the proposed production site were provided for 2 pilot scale batches for each concentration. The results of all tests are well within specification limits and batch data is acceptable

- **Container closure system**

- The drug product is packed in triplex (OPA/ AL/ PVC /AL) blister then further placed in a carton box with an inner leaflet.

- **Stability**

- Stability of finished pharmaceutical product is submitted in accelerated ($40^{\circ}\text{C} \pm 2^{\circ}\text{C}$ /75% RH $\pm$ 5% RH) and long-term ($30^{\circ}\text{C} \pm 2^{\circ}\text{C}$ /65% RH $\pm$ 5% RH) storage conditions. Detailed review was carried out for all stability indicating parameters and all found in line with their acceptance criteria throughout all time intervals. The finished pharmaceutical product is stable for 24 months if stored below 30°C in a dry place.
- Specific measures concerning the prevention of the transmission of animal spongiform encephalopathies

- There are no substances of ruminant animal origin present in the product nor have any been used in the manufacturing of this product, so a theoretical risk of transmitting TSE can be excluded.
- A declaration/certificate of TSE/BSE free is submitted for Magnesium Stearate

Summary basis of opinion:

From Chemistry, Manufacture and Control perspective, the main concerns found during the evaluation process were as follow:

For the Drug substance:

-The quality of the drug substance is considered to be acceptable when used in accordance with the conditions defined.

For the Drug product:

- Kindly omit “Water content limit will be re-evaluated after long term stability study” & tighten the limit for water content based on the final interval tested.

The Quality of the drug product has been found satisfactory after

- The applicant has revised the specifications of the drug product to limit for water content based on the final interval tested

III. Non-Clinical

No new preclinical data have been submitted with this application. As such, no pre-clinical assessment has been made on the application. This is acceptable for this type of application. An Environmental Risk Assessment has not been performed as this product is intended for generic substitution and therefore will not result in an increase of risk to the environment during use, storage and disposal.

IV. Clinical Aspects

Introduction

Mirogabalin name is a well-known active substance with established efficacy and tolerability. A clinical overview has been provided, which is based on scientific literature.

Mirogabalin is indicated for patients with diabetic peripheral neuropathic pain (DPNP) and postherpetic neuralgia (PHN), for the indication of peripheral neuropathic pain (PNP)

Pharmacokinetics

Bioequivalence Study

The bioequivalence study of Miroxnoric 15 mg F.C.Tablets Man. by: P&C Labs (Pellets&CR Products), Egypt relative to Tarlige 15 mg Tablets by Daiichi Sankyo Co., Limited, Japan administered to healthy subjects.

Biowaiver

The EDA was granted a biowaiver for the lower strength Miroxnoric 2.5 ,5 and 10 mg F.C.Tablets based on the following arguments;

all tablets strengths have comparable dissolution profiles according to the provided in vitro dissolution data.

Design

Open-label, randomized, two-way crossover study to compare the relative bioavailability of Mirogabalin from Miroxnoric 15 mg F.C.Tablets (Man. by: P&C Labs (Pellets&CR Products), Egypt) and Tarlige 15 mg Tablets (Daiichi Sankyo Co., Limited, Japan) given as a single dose under Fasting Conditions with a Washout Period of 7 days Between periods in healthy subjects.

Analytical Methods

All procedures used to perform the bio-analyses of Mirogabalin in subject samples were executed according to international guidelines and official publications.

CRO developed an adequately validated method to ensure data integrity, Accuracy and Precision of data generated during sampling, sample treatment and bioanalyses. The bioequivalence study accordance with acceptable standards of Good Clinical Practice (GCP) and Good Laboratory Practice (GLP).

Results

Table 1. Pharmacokinetic parameters (non-transformed values; arithmetic mean $\pm$ SD, $t_{\max}$ (median, range) of Miroxnoric 15 mg F.C.Tablets under fasting conditions.

Treatment N=28	AUC _{0-t} ng.h/ml	AUC _{0-∞} ng.h/ml	C _{max} ng/ml	t _{max} h	t _{1/2} h
Test	1123.10 $\pm$ 560.50	1148.27 $\pm$ 580.02	261.32 $\pm$ 104.38	1.51 $\pm$ 0.69 (0.5-3.00)	3.94 $\pm$ 1.24
Reference	1133.92 $\pm$ 522.47	1146.89 $\pm$ 522.25	248.97 $\pm$ 105.01	1.60 $\pm$ 0.76 (0.5-3.5)	3.71 $\pm$ 0.71
*Ratio (90%) CI	98.18 (92.96- 103.70)	98.89 (93.46- 104.64)	106.06 (99.98- 112.51)	-----	-----
CV (%)	-----	-----	-----	-----	-----

*ln-transformed values

Conclusion

The 90% confidence intervals calculated for AUC_{0-t} and C_{max} are within the bioequivalence acceptance range of 80-125%.

Based on this study demonstrated that the Mirogabalin in tablet form of the Miroxnoric 15 mg F.C.Tablets Man. by: P&C Labs (Pellets&CR Products), Egypt & Tarlige 15 mg Tablets by Daiichi Sankyo Co., Limited, Japan are Bioequivalent after a single oral dose of test and reference administration under Fasting conditions on 28 healthy volunteers.