Public Assessment Report

Decentralised Procedure

Capsorin 25, 50 and 100 mg soft capsules

(ciclosporin)

UK/H/0981/001-03/DC

UK licence no: PL 20117/0036-0038

Morningside Healthcare Ltd

LAY SUMMARY
Capsorin 25, 50 and 100 mg soft capsules (ciclosporin)

This is a summary of the public assessment report (PAR) for Capsorin 25, 50 and 100 mg soft capsules (UK/H/0981/001-03/DC; PL 20117/0036-0038). These medicinal products will be referred to as Capsorin capsules in the remainder of this summary, for ease of reading.

This summary explains how Capsorin capsules were assessed and their authorisations recommended as well as their conditions of use. It is not intended to provide practical advice on how to use these products.

For practical information about Capsorin capsules, patients should read the package leaflets or contact their doctor or pharmacist.

What are Capsorin capsules and what are they used for?
Capsorin capsules are 'generic medicines'. This means that Capsorin capsules are similar to 'reference medicines' already authorised in the UK called Neoral Soft Gelatin Capsules 25 mg, 50 mg and 100 mg (Novartis Pharmaceuticals UK Ltd; PL 00101/0387-0389).

Capsorin capsules are used to lower the body's immune reactions. These medicinal products control body's immune system following an organ transplant, bone marrow and stem cell transplantation.

Capsorin also stops an autoimmune disease (when the body's immune response attacks its own cells). Such diseases include eye problems which threaten the vision (endogenous uveitis, including Behcet's uveitis), severe cases of certain skin diseases (atopic dermatitis or eczema and psoriasis), severe rheumatoid arthritis and a kidney disease called nephrotic syndrome.

How are Capsorin capsules used?
Capsorin capsules are taken by mouth. A whole capsule should be swallowed with water at the same time every day.

The daily doses should always be divided into two.

In adult:
Organ, bone marrow and stem cell transplantation

- The total dose each day is usually between 2 mg and 15 mg per kilogram body weight.
- Usually, higher doses are used before and just after the transplant. Lower doses are used once the transplanted organ or bone marrow has stabilised.
- A doctor will adjust the dose to one that is ideal for the patient by taking blood tests.

Endogenous uveitis

- The total dose each day is usually between 5 mg and 7 mg per kilogram body weight.

Nephrotic syndrome

- The total dose each day for adults is usually 5 mg per kilogram body weight. In patients with kidney problem, the first dose taken each day should not be more than 2.5 mg per kilogram body weight.

Severe rheumatoid arthritis

- The total dose each day is usually between 3 and 5 mg per kilogram body weight.

In children:

Nephrotic syndrome

- The total dose each day for children is usually 6 mg per kilogram body weight. In patients with kidney problems, the first dose taken each day should not be more than 2.5 mg per kilogram body weight.

These medicinal products can only be obtained on prescription from a doctor.

For further information on how Capsorin capsules are used, refer to the Summaries of Product Characteristics or package leaflet available on the MHRA website.

How do Capsorin capsules work?

Capsorin capsules contain the active substance, ciclosporin, which belongs to a group of medicines known as immunosuppressive agents. Capsorin prevents rejection of transplanted organs by blocking the development of certain cells which would normally attack the transplanted tissue.

How have Capsorin capsules been studied?

Because Capsorin capsules are generic medicines, studies in patients have been limited to tests to determine that they are bioequivalent to the reference medicines, Neoral® 25 mg, 50 mg and 100 mg soft gelatine capsules marketed in France (Novartis Pharma S.A.S., France), which is equivalent to Neoral Soft Gelatin Capsules 25 mg, 50 mg and 100 mg (Novartis Pharmaceuticals UK Ltd). Two medicines are bioequivalent when they produce the same levels of the active substance in the body.

What are the benefits and risks of Capsorin capsules?

As Capsorin capsules are generic medicines that are bioequivalent to Neoral® 25 mg, 50 mg and 100 mg soft gelatine capsules, their benefits and risks are taken as being the same as those for Neoral® 25 mg, 50 mg and 100 mg soft gelatine capsules.

Why are Capsorin capsules approved?

It was concluded that, in accordance with EU requirements, Capsorin capsules have been shown to have comparable quality and are bioequivalent to Neoral® 25 mg, 50 mg and 100 mg soft gelatine capsules. Therefore, the view was that, as for Neoral® 25 mg, 50 mg and 100 mg soft gelatine capsules the benefit outweighs the identified risk.

What measures are being taken to ensure the safe and effective use of Capsorin capsules?

A satisfactory pharmacovigilance system has been provided to ensure that Capsorin capsules are used as safely as possible. Based on this plan, safety information has been included in the Summaries of Product Characteristics and the package leaflet for Capsorin capsules, including the appropriate precautions to be followed by healthcare professionals and patients.

Other information about Capsorin capsules

Greece, Slovak Republic and the UK agreed to grant Marketing Authorisations for Capsorin capsules on 9th November 2007. Marketing Authorisations were granted in the UK on 13th February 2008.

The full PAR for Capsorin capsules follows this summary. For more information about treatment with Capsorin capsules, read the package leaflet or contact your doctor or pharmacist.

This summary was last updated in April 2015.

TABLE OF CONTENTS

I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the UK granted Marketing Authorisations for the medicinal products Capsorin 25 mg, soft capsules (PL 20117/0036), Capsorin 50 mg, soft capsules (PL 20117/0037) and Capsorin 100 mg, soft capsules (PL 20117/0038) on 13 February 2008. The products are prescription only medicines.

These applications were made under Article 10.1 of Directive 2001/83 EC, as amended, claiming that Capsorin 25 mg, 50 mg and 100 mg soft capsules are generic products of Sandimmun Optoral 25 mg, 50 mg and 100 mg capsules (Novartis, Germany) which were authorised in May 1994. The UK reference products are Neoral Soft Gelatin Capsules 25 mg, 50 mg and 100 mg (Novartis Pharmaceuticals UK Ltd, trading as Sandoz Pharmaceuticals; PL 00101/0387-0389), which were granted licenses in March 1995. The reference products have therefore been authorised in the EEA for at least 10 years.

The products contain the active ingredient ciclosporin and are indicated in combination with other immunosuppressant substances for the prevention of acute and chronic transplant rejection following allogenic transplantation of kidneys, liver, heart, heart-lung, lung or pancreas. The products are also indicated for the prevention and treatment of graft-versus-host-disease (GVHD) following allogenic bone marrow transplantation as well as for the treatment of severe forms of psoriasis, atopic dermatitis and active rheumatoid arthritis.

Ciclosporin is a polypeptide which produces a specific and reversible inhibition of T lymphocytes in G0 and G1 cellular phase. Unlike cytostatics, ciclosporin does not suppress haematopoiesis and has no effects under phagocytic cells. As a result of this mechanism of action, ciclosporin has been widely used to prevent and treat the rejection of GVHD in bone marrow and solid organ transplants. Additionally, ciclosporin has beneficial effects in a wide range of autoimmune pathologies, such as rheumatoid arthritis, psoriasis and atopic dermatitis.

No new non-clinical studies were conducted, which is acceptable given that the applications referred to products that have been licensed for over 10 years.

No clinical studies were conducted, which is acceptable given that the applications referred to products that have been licensed for over 10 years. The bioequivalence studies were carried out in accordance with Good Clinical Practice (GCP).

The RMS has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for this product type at all sites responsible for the manufacture and assembly of these products. Evidence of compliance with GMP has been provided for the named manufacturing and assembly sites.

The decentralised procedure was completed at Day 210 (08 November 2007), with the reference member state (RMS) and the concerned member states (CMSs) agreeing that the licences were approvable. The national phase of the decentralised procedure was completed in the UK on 13 February 2008.

II QUALITY ASPECTSDRUG SUBSTANCE

All aspects of the manufacture and control of ciclosporin are supported by a European Directorate for the Quality of Medicines Healthcare (EDQM) Certificate of Suitability. This certificate is accepted as confirmation of the suitability of ciclosporin for inclusion in these medicinal products.

Appropriate stability data have been provided to support a retest period of 4 years when stored in the proposed packaging.

DRUG PRODUCT

Other Ingredients

The excipients present are ethanol anhydrous, tocopherol acetate, diethylene glycol monoethyl ether, oleoyl macrogolglycerides and macrogolglycerol hydroxystearate. Gelatin, glycerol, propylene glycol, titanium dioxide (E171), black iron oxide (E172) (25 mg and 100 mg capsules only) and purified water are also present in the capsule shell.

The excipients used comply with their respective European Pharmacopoiea monographs. Satisfactory Certificates of Analysis have been provided.

Gelatin is the only excipient that contains material of animal or human origin. A Transmissible Spongiform Encephalopathies (TSE) Certificate has been provided for gelatin confirming that the risk of transmitting TSE is sufficiently low.

Pharmaceutical Development

The applicant has provided suitable product development rationale and data.

Impurity Profile

Comparative impurity profiles for the German reference product and test product are provided. The test product has a lower total impurity content than the reference product.

Dissolution Profile

Comparative dissolution profiles were generated for the reference product (Neoral 100 mg soft gelatine capsules, Novartis, Germany), reference biobatch (Neoral 100 mg soft gelatine capsules, Novartis, France) and test biobatch (Capsorin 100 mg, soft capsules). The dissolution method used was chosen as it is the most discriminative.

Manufacture

Satisfactory batch formulae have been provided for the manufacture of the products along with an appropriate account of the manufacturing process. Suitable in-process controls are applied during the manufacturing process to ensure the quality of the product.

The manufacturing process has been validated and the results are satisfactory.

Control of Drug Product

The proposed finished product specifications are acceptable and provide an assurance of the quality of the finished product. The analytical methods used have been suitably

validated. Batch analysis data have demonstrated compliance with the proposed specification.

Reference Standards or Materials
Certificates of Analysis for all reference standards used have been provided and are satisfactory.

Container Closure System
The finished product is packaged in aluminium-aluminium blisters in pack sizes of 10, 20, 30, 50 and 60 capsules. Satisfactory specifications and Certificates of Analysis have been provided for the packaging components. All primary product packaging complies with EU legislation regarding contact with food.

Stability of the Drug Product
The stability data provided support a shelf-life of 3 years, with storage conditions "Store in the original package in order to protect from light and moisture".

Bioequivalence/Bioavailability
Refer to the clinical assessment.

Conclusion
It is recommended that Marketing Authorisations are granted for these applications.

III NON-CLINICAL ASPECTS

The pharmacodynamic, pharmacokinetic and toxicological properties of ciclosporin are well known. As ciclosporin is a widely used, well known active substance, the applicant has not provided additional studies and further studies are not required. An overview based on a literature review is therefore appropriate.

The non-clinical overview has been written by an appropriately qualified pharmacist and is a concise summary of the literature reviewed. In view of the fact that ciclosporin is a well-known compound it is adequate.

Section 5.3 of the SmPCs is identical to those of the reference medicinal products.

Conclusions

Ciclosporin is a well-known active substance. The proposed indications are stated to be identical to the authorised indication for the reference products.

There are no objections to the approval of Capsorin 25 mg, 50 mg and 100 mg soft capsules.

IV CLINICAL ASPECTS

Pharmacokinetics

Ciclosporin is distributed largely outside the blood volume. In the blood, 33-47% is present in plasma, 4-9% in lymphocytes, 5-12% in granulocytes, and 41-58% in erythrocytes. In plasma, approximately 90% is bound to proteins, mostly lipoproteins.

Ciclosporin is extensively biotransformed to approximately 15 metabolites. There is no single major metabolic pathway. Elimination is primarily biliary, with only 6% of the oral dose excreted in the urine; only 0.1% is excreted in the urine as unchanged drug.

There is a high variability in the data reported on the terminal half-life of ciclosporin depending on the assay applied and the target population. The terminal half-life ranged from 6.3 hours in healthy volunteers to 20.4 hours in patients with severe liver disease.

To support the applications, the applicant has submitted two bioequivalence studies (fasting and fed conditions) comparing the test product with the reference product.

The excipient ratio, manufacturing process/site and dissolution profile criteria support the use of single dose strength studies to confirm bioequivalence. With reference to the requirement for linear pharmacokinetics to support single dose strength studies, the pharmacokinetic linearity of the reference product has been demonstrated over a wide, clinically relevant range (approximately 200-800mg). Given the similarity of the test formulation to the reference product, linear pharmacokinetic (PK) can reasonably be expected for the Applicant's products.

Study 1

This was a randomized, open-label, 2-way crossover, bioequivalence study of Capsorin 100 mg soft capsules and Neoral 100 mg soft gelatine capsules from Novartis Pharma S.A.S., France (Reference) following a 200 mg dose in healthy subjects under fasting conditions.

A single oral dose of ciclosporin as 2 x 100 mg capsules was administered in each study period under fasting conditions. The treatment phases were separated by a washout period of 14 days. Blood samples were collected prior to study drug administration and 0.333, 0.667, 1.00, 1.25, 1.50, 1.75, 2.00, 2.50, 3.00, 3.50, 4.00, 6.00, 8.00, 12.0, 16.0, 24.0, 36.0, and 48.0 hours postdose in each period.

Analytical method:

Whole blood samples were analysed using Liquid Chromatography MS using a calibration curve range of 5.05 ng/ml to 1516.10 ng/ml.

The statistical methods used were:

Pharmacokinetics:

- Parametric ANOVA on AUC_{0-t}, AUC_{0-inf}, C_{max}, $T_{1/2\ el}$ and K_{el}; geometric confidence intervals for AUC_{0-t}, AUC_{0-inf} and C_{max}; and non-parametric test (Wilcoxon) for T_{max};

- Covariates in the ANOVA model: sequence, subject within sequence, period and treatment;
- Ln-transformed parameters: AUC_{0-t}, AUC_{0-inf} and C_{max}.

Criteria for Bioequivalence:
For both potency corrected and uncorrected data: 90% geometric confidence intervals of the ratio (A/B) of least-squares means from the ANOVA of the ln-transformed AUC0-t and Cmax should be within 80% to 125%.

Results:

Parameters		Test (Cyclosporine (A)) Mean	±	SD	CV (%)	Reference (Neoral (B)) Mean	±	SD	CV (%)
AUC_{0-t}	(ng·h/mL)	4124.94	±	940.73	22.81	4227.06	±	946.34	22.39
AUC_{0-inf}	(ng·h/mL)	4257.27	±	983.82	23.11	4370.34	±	997.26	22.82
C_{max}	(ng/mL)	1050.17	±	217.96	20.75	1079.25	±	214.48	19.87
Residual area	(%)	3.04	±	0.88	29.08	3.18	±	1.26	39.49
T_{max}	(h)	1.43	±	0.30	21.02	1.48	±	0.48	32.36
T_{max}*	(h)	1.50	±	0.50	-	1.50	±	0.25	-
K_{el}	(h^{-1})	0.0578	±	0.0128	22.19	0.0564	±	0.0144	25.59
$T_{½\ el}$	(h)	12.53	±	2.58	20.61	13.03	±	3.11	23.91

* Medians and interquartile ranges are presented.

A significant sequence effect was detected for the Test product. However, there was no detectable pre-dose concentration and there was no significant increase in PK parameters from period 1 to 2 indicating there is no evidence of carryover.

The residual area was calculated for each subject and treatment. The mean percentage of extrapolated area under the curve was lower than 20% for all treatments indicating that duration of blood sampling was adequate.

PK calculations were also performed on data corrected for measured content and the results are shown below.

Statistical Analysis (Potency corrected)	Ratio (Test/Reference)	90% Geometric CI
AUC_{0-t}	90.33%	95.95-102.83
$AUC_{0-\infty}$	99.18%	95.79-102.68
C_{max}	99.19%	94.17-104.48

Safety
45 post-dose adverse events (AEs) occurred during the study, most of them rated as mild and few moderate. Of these, 31 were considered to be potentially related to the study medication: 12 (38.7%) following administration of test treatment and 18 (58.1

%) following admninistration of reference treatment. The most commonly reported AEs were "Headache", "Nausea", and "Vasodilat". No serious or significant adverse events were reported during this study.

Study 2

This was a randomized, open-label, 2-way crossover, bioequivalence study of Capsorin 100 mg soft capsules and Neoral 100 mg soft gelatine capsules from Novartis Pharma S.A.S., France (Reference) following a 200 mg dose in healthy subjects under fed conditions.

A single oral dose of ciclosporin as 2 x 100 mg capsules was administered in each study period under fed conditions. The treatment phases were separated by a washout period of 14 days. Blood samples were collected prior to study drug administration and 0.333, 0.667, 1.00, 1.25, 1.50, 1.75, 2.00, 2.50, 3.00, 3.50, 4.00, 6.00, 8.00, 12.0, 16.0, 24.0, 36.0, and 48.0 hours postdose in each period.

Analytical method:

Whole blood samples were analysed using Liquid Chromatography MS using a calibration curve range of 5.05 ng/ml to 1516.10 ng/ml.

The statistical methods used were:

Pharmacokinetics:

- Parametric ANOVA on AUC_{0-t}, AUC_{0-inf}, C_{max}, $T_{1/2\ el}$ and K_{el}; geometric confidence intervals for AUC_{0-t}, AUC_{0-inf} and C_{max}; and non-parametric test (Wilcoxon) for T_{max};
- Covariates in the ANOVA model: sequence, subject within sequence, period and treatment;+

- Ln-transformed parameters: AUC_{0-t}, AUC_{0-inf} and C_{max}.

Criteria for Bioequivalence:

For both potency corrected and uncorrected data: 90% geometric confidence intervals of the ratio (A/B) of least-squares means from the ANOVA of the ln-transformed AUC_{0-t} and C_{max} should be within 80% to 125%.

Results:

Parameters		Test (Cyclosporine (A)) Mean	±	SD	CV (%)	Reference (Neoral (B)) Mean	±	SD	CV (%)
AUC_{0-t}	(ng·h/mL)	3995.82	±	1125.03	28.16	4094.57	±	878.19	21.45
AUC_{0-inf}	(ng·h/mL)	4109.72	±	1159.39	28.21	4209.65	±	908.15	21.57
C_{max}	(ng/mL)	1069.72	±	407.88	38.13	1020.20	±	321.49	31.51
Residual area	(%)	2.78	±	0.76	27.31	2.71	±	0.74	27.28
T_{max}	(h)	1.65	±	0.80	48.34	1.60	±	0.60	37.62
T_{max}*	(h)	1.50	±	0.38	-	1.50	±	0.50	-
K_{el}	(h^{-1})	0.0611	±	0.0229	37.47	0.0611	±	0.0204	33.33
$T_{½\ el}$	(h)	12.25	±	2.70	22.07	12.13	±	2.61	21.54

* Medians and interquartile ranges are presented.

The residual area was calculated for each subject and treatment. The mean percentage of extrapolated area under the curve was lower than 20% for all treatments indicating that the duration of blood sampling was sufficient.

Pharmacokinetic (PK) calculations were performed on potency corrected (shown below) and uncorrected data. All PK calculations showed the 90% CI for AUC and C_{max} within the acceptance limits of 80%-125%.

Statistical Analysis (Potency corrected)	Ratio (Test/Reference)	90% Geometric CI
AUC_{0-t}	97.46%	87.81-108.17
$AUC_{0-\infty}$	97.53%	87.92-108.20
C_{max}	103.75%	87.79-122.61

Safety

68 post-dose adverse events (AEs) occurred during the study, 46 graded as mild and 14 as moderate. Of these, 50 were judged to be potentially related to the study medication: 24 (48.0%) following administration of test treatment and 19 adverse events (38.0 %) following administration of reference treatment. Of the potentially related AEs, the most commonly reported adverse events were “Headache”, “Pharyngitis” and “Vasodilat”. No serious adverse events were reported during this study.

Conclusion

Based on the submitted bioequivalence studies, Ciclosporin 100 mg soft capsules are considered to be bioequivalent to the reference product. Performing the two studies (under fed and fasting conditions) has shown a good comparative in terms of bioequivalence between the test product and the reference product. The design and the method of the studies are satisfactory.

Pharmacodynamics

Ciclosporin is a potent immunosuppressive agent which prolongs survival of allogeneic transplants involving skin, heart, kidney, pancreas, bone marrow, small intestine and lung in animals. On a cellular level it inhibits the liberation of lymphocytes including interleukin 2(T-cells growth factor, TCGF). As it appears, ciclosporin blocks the lymphocytes during phase G0 or G1 of the cellular cycle and inhibits the release of lymphokines unbound by antigens, by activated T-cells.

All of the evidence shows that ciclosporin acts specifically and in a reversible manner upon the lymphocytes. Contrary to cytostatic agents, ciclosporin does not depress the hematopoiesis and has no effect on the phagocytic cells.

Bone marrow transplants and solid organ transplants in humans have been accomplished with great success using ciclosporin for microemulsion to prevent and treat rejections and graft-versus-host-disease (GVHD). There have also been beneficial effects noted in ciclosporin therapy of various auto-immune diseases.

No new pharmacodynamic data have been submitted and none are required for this application.

EFFICACY
No new efficacy data have been provided and none are required for applications of this type.

SAFETY
No new safety data have been provided and none are required for applications of this type.

EXPERT REPORT
A satisfactory clinical expert report has been submitted, which has been written by an appropriately qualified medical doctor.

SUMMARIES OF PRODUCT CHARACTERISTICS (SmPCs)
These are satisfactory and consistent with the SmPCs for the reference products.

PATIENT INFORMATION LEAFLET (PIL)
This is satisfactory and consistent with the SmPCs.

LABELLING
These are satisfactory.

The Marketing Authorisation Holder has provided adequate justification for not submitting a detailed Risk Management Plan (RMP).

CONCLUSION
The applications contain an adequate review of published clinical data and bioequivalence has been shown. Approval is recommended from the clinical point of view. Conducting bioequivalence studies across the range of indications is accepted as difficult and therefore the results seen in healthy volunteers are considered sufficient for approval. However, an adequate post-marketing study addressing surveillance of acute graft rejection rates and renal function for a defined period following treatment with Capsorin 25 mg, 50 mg and 100 mg soft capsules is considered necessary.

V. User consultation

The package leaflet has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC, as amended. The language used for the purpose of user testing the package leaflet was English.

The results show that the package leaflet meets the criteria for readability as set out in the *guideline on the readability of the label and package leaflet of medicinal products for human use.*

VI OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT AND RECOMMENDATION

QUALITY

The important quality characteristics of Capsorin 25 mg, 50 mg and 100 mg soft capsules are well-defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

NON-CLINICAL

No new non-clinical data were submitted and none are required for applications of this type.

CLINICAL

Bioequivalence has been demonstrated between the applicant's Capsorin 100 mg soft capsules and Neoral 100 mg soft gelatine capsules (Novartis Pharma S.A.S., France). Given that linear kinetics apply between the 25 mg, 50 mg and 100 mg capsules, that proportional formulae for the capsules have been used, the method of manufacture is the same and that similar dissolution results have been shown for the three strengths, separate bioequivalence studies using the 25 mg and 50 mg capsules are not considered necessary.

No new or unexpected safety concerns arose from these applications.

The SmPCs, PIL and labelling are satisfactory and consistent with those for the reference products.

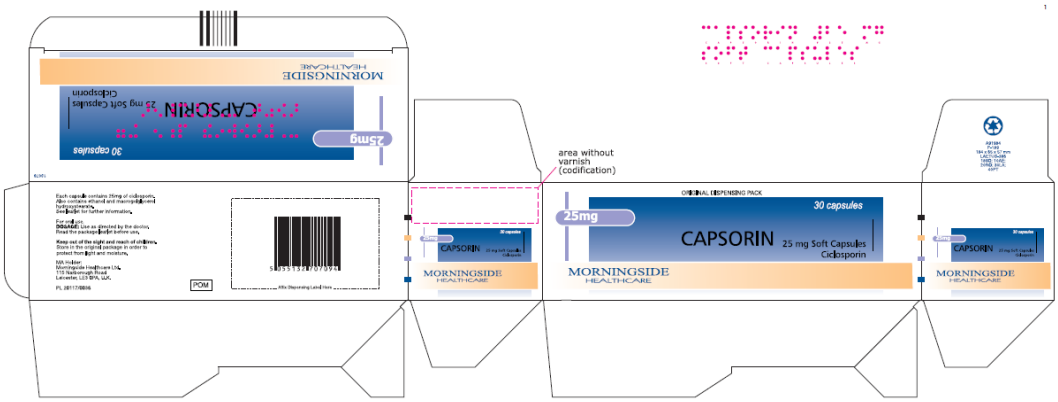
BENEFIT RISK ASSESSMENT

The quality of the products is acceptable and no new non-clinical or clinical concerns have been identified. The bioequivalence studies support the claim that the applicant's products and the reference products are interchangeable. Clinical experience with ciclosporin is considered to have demonstrated the therapeutic value of the compound. The benefit risk is, therefore, considered to be positive.

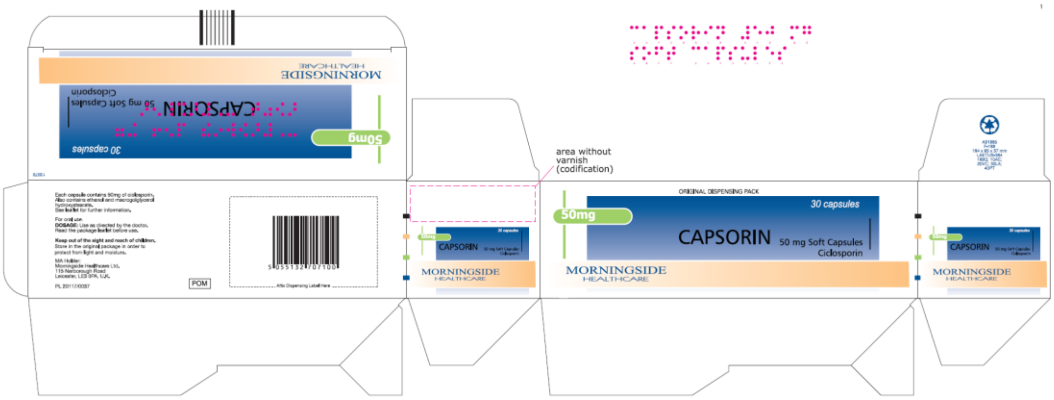
Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling

In accordance with Directive 2010/84/EU the Summaries of Product Characteristics (SmPCs) and Patient Information Leaflets (PILs) for products that are granted Marketing Authorisations at a national level are available on the MHRA website.

LABELLING



Capsorin
25mg Soft Capsules
(Ciclosporin)
MORNINGSIDE HEALTHCARE LTD



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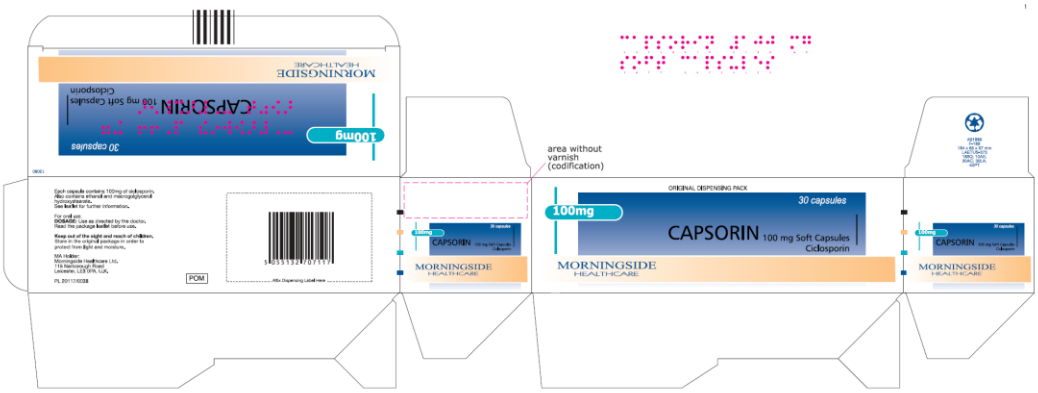
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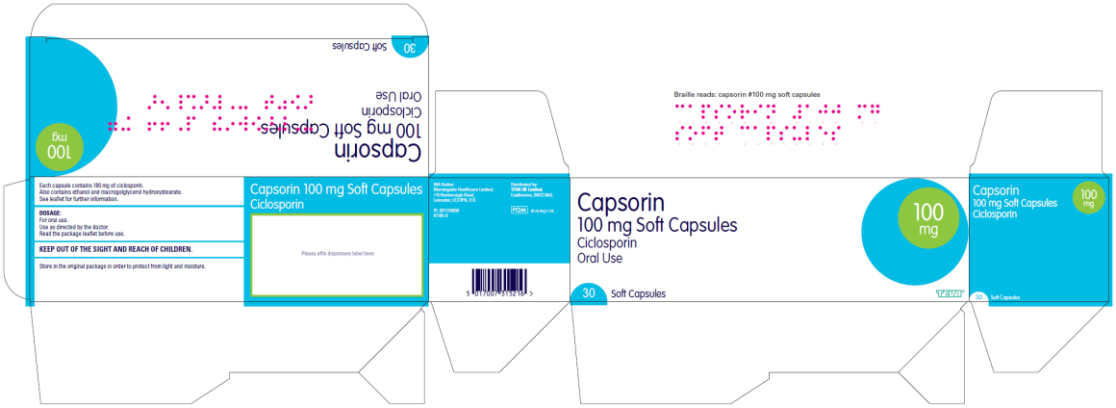
100mg
30 capsules
CAPSORIN 100 mg Soft Capsules Ciclosporin
MORNINGSIDE HEALTHCARE
POM


Capsorin 100 mg Soft Capsules Ciclosporin
Oral Use
30 Soft capsules
100 mg
Each capsule contains 100 mg of ciclosporin.
Also contains ethanol and macrogolglycerol hydroxystearate.
See leaflet for further information.
DOSAGE:
For oral use.
Use as directed by the doctor.
Read the package leaflet before use.
KEEP OUT OF THE SIGHT AND REACH OF CHILDREN.
Store in the original package in order to protect from light and moisture.
Capsorin 100 mg Soft Capsules
Ciclosporin
Please affix dispensary label here
Capsorin
100 mg Soft Capsules
Ciclosporin
Oral Use
30 Soft Capsules
100 mg
Capsorin
100 mg Soft Capsules
Ciclosporin
100 mg

Capsorin ***100mg Soft Capsules*** *(Ciclosporin)* **MORNINGSIDE HEALTHCARE LTD**	***Capsorin*** ***100mg Soft Capsules*** *(Ciclosporin)* **MORNINGSIDE HEALTHCARE LTD**	***Capsorin*** ***100mg Soft Capsul*** *(Ciclosporin)* **MORNINGSIDE HEALTH**
Capsorin ***100mg Soft Capsules*** *(Ciclosporin)* **MORNINGSIDE HEALTHCARE LTD**	***Capsorin*** ***100mg Soft Capsules*** *(Ciclosporin)* **MORNINGSIDE HEALTHCARE LTD**	***Capsorin*** ***100mg Soft Capsul*** *(Ciclosporin)* **MORNINGSIDE HEALTH**
Capsorin ***100mg Soft Capsules*** *(Ciclosporin)* **MORNINGSIDE HEALTHCARE LTD**	***Capsorin*** ***100mg Soft Capsules*** *(Ciclosporin)* **MORNINGSIDE HEALTHCARE LTD**	***Capsorin*** ***100mg Soft Capsul*** *(Ciclosporin)* **MORNINGSIDE HEALTH**
Capsorin ***100mg Soft Capsules*** *(Ciclosporin)* **MORNINGSIDE HEALTHCARE LTD**	***Capsorin*** ***100mg Soft Capsules*** *(Ciclosporin)* **MORNINGSIDE HEALTHCARE LTD**	***Capsorin*** ***100mg Soft Capsul*** *(Ciclosporin)* **MORNINGSIDE HEALTH**
Capsorin ***100mg Soft Capsules*** *(Ciclosporin)* **MORNINGSIDE HEALTHCARE LTD**	***Capsorin*** ***100mg Soft Capsules*** *(Ciclosporin)* **MORNINGSIDE HEALTHCARE LTD**	***Capsorin*** ***100mg Soft Capsul*** *(Ciclosporin)* **MORNINGSIDE HEALTH**
Capsorin ***100mg Soft Capsules*** *(Ciclosporin)* **MORNINGSIDE HEALTHCARE LTD**	***Capsorin*** ***100mg Soft Capsules*** *(Ciclosporin)* **MORNINGSIDE HEALTHCARE LTD**	***Capsorin*** ***100mg Soft Capsul*** *(Ciclosporin)* **MORNINGSIDE HEALTH**
Capsorin ***100mg Soft Capsules*** *(Ciclosporin)* **MORNINGSIDE HEALTHCARE LTD**	***Capsorin*** ***100mg Soft Capsules*** *(Ciclosporin)* **MORNINGSIDE HEALTHCARE LTD**	***Capsorin*** ***100mg Soft Capsul*** *(Ciclosporin)* **MORNINGSIDE HEALTH**
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Capsorin ***100mg Soft Capsules*** *(Ciclosporin)* **MORNINGSIDE HEALTHCARE LTD**	***Capsorin*** ***100mg Soft Capsules*** *(Ciclosporin)* **MORNINGSIDE HEALTHCARE LTD**	***Capsorin*** ***100mg Soft Capsul*** *(Ciclosporin)* **MORNINGSIDE HEALTH**

Table of content of the PAR update for MRP and DCP

Steps taken after the initial procedure with an influence on the Public Assessment Report

The following table lists some non-safety updates to the Marketing Authorisations for these products that have been approved by the MHRA since the products were first licensed. The table includes updates that are detailed in the annex to this PAR. This is not a complete list of the post-authorisation changes that have been made to these Marketing Authorisations.

Scope	Procedure number	Product information affected	Date of start of the procedure	Date of end of procedure	Approval/ non approval	Assessment report attached Y/N (version)
To update sections 1 (Name of the medicinal product), 2 (Qualitative and quantitative composition), 3 (Pharmaceutical form), 4 (Clinical particulars), 5 (Pharmacological properties), 6.4 (Special precautions for storage), 6.5 (Nature and content of container) and 6.6 (Special precautions for disposal) of the SmPC and consequentially the leaflet in line with the Commission Decisions C(2013)6347 and C(2013)7503 and also the QRD template.	UK/H/0981/001-03/IB/030	SmPC and PIL	28/11/2014	16/03/2015	Approval	Yes

Annex 1

Reference: **PL 20117/0036-0052; PL 20117/0037-0049; PL 20117/0038-0049**

Product: **Capsorin 25, 50 and 100 mg soft Capsules**

MAH: **Morningside Healthcare Ltd**

Active Ingredient: **Ciclosporin**

Reason:
To update sections 1 (Name of the medicinal product), 2 (Qualitative and quantitative composition), 3 (Pharmaceutical form), 4 (Clinical particulars), 5 (Pharmacological properties), 6.4 (Special precautions for storage), 6.5 (Nature and content of container) and 6.6 (Special precautions for disposal) of the SmPC and consequentially the leaflet in line with the Commission Decisions C(2013)6347 and C(2013)7503 and also the QRD template.

Supporting evidence
The applicant has submitted updated sections of the SmPCs and the leaflet.

Evaluation
The amended sections of the SmPCs and the leaflet mock-up are satisfactory.

Conclusion
The variation was approved on 16th March 2015 and the updated SmPCs fragments and the PIL have been incorporated into these Marketing Authorisations. The proposed changes are acceptable.

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC) Updated

Following approval of the variation on 16th March 2015 the SmPCs were updated. In accordance with Directive 2010/84/EU the Summaries of Product Characteristics (SmPCs) for products that have been granted Marketing Authorisations at a national level are available on the MHRA website.

PATIENT INFORMATION LEAFLET (PIL) - Updated

Following approval of the variation on 16th March 2015 the PIL was updated. In accordance with Directive 2010/84/EU the Patient Information Leaflet (PIL) for products that have been granted Marketing Authorisations at a national level are available on the MHRA website.