The MHRA has granted Dexcel Pharma Ltd Marketing Authorisations (licences) for the medicinal products Risperidone 0.5mg, 1mg, 2mg, 3mg, 4mg and 6mg Film-Coated Tablets (PL 14017/0130-5). These are prescription-only medicines (POM).

Risperidone Tablets are one of a group of medicines called antipsychotics. They are used to treat conditions which affect the way you think, feel and/or act. These conditions may cause symptoms such as confusion, hallucinations (e.g. hearing, seeing or sensing things which are not there), delusions, unusual suspiciousness (paranoia) and emotional and social withdrawal. People with these conditions may also feel depressed, guilty, anxious or tense. Risperidone Tablets may be taken for both sudden (acute) and long-lasting (chronic) disorders.

In addition, Risperidone Tablets may be used to control the symptoms of mania for people with bipolar disorder.

No new or unexpected safety concerns arose from these applications and it was therefore judged that the benefits of taking Risperidone 0.5mg, 1mg, 2mg, 3mg, 4mg, and 6mg Film-coated Tablets outweighs the risks, hence Marketing Authorisations have been granted.
Risperidone 0.5, 1, 2, 3, 4 and 6mg Film-Coated Tablets

PL 14017/0130-5

Scientific Discussion

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Pharmaceutical assessment  Page 5
Preclinical assessment  Page 8
Clinical assessment (including statistical assessment)  Page 9
Overall conclusions and risk benefit assessment  Page 11
INTRODUCTION

Based on the review of the data on quality, safety and efficacy the UK granted marketing authorisations for the medicinal products Risperidone 0.5mg, 1mg, 2mg, 3mg, 4mg, and 6mg Film-coated Tablets on 16th of October 2007. The products are prescription only medicines.

These applications were submitted as an abridged applications according to Article 10(1) of Directive 2001/83/EC, claiming to be a generic medicinal product of the original products Risperdal 1mg tablets (PL 00242/0186), Risperdal 2mg tablets (PL 00242/0187), Risperdal 3mg tablets (PL 00242/0188) and Risperdal 4mg tablets (PL 00242/0189) first authorised in UK in December 1992 to Janssen-Cilag Ltd.

Risperidone is a novel antipsychotic belonging to a new class of antipsychotic agents, the benzisoxazole-derivatives.

The products contain the active ingredient risperidone and are indicated for the treatment of acute and chronic schizophrenic psychoses and other psychotic conditions in which positive symptoms (such as hallucinations, delusions, thought disturbances, hostility, suspiciousness), and/or negative symptoms (such as blunted affect, emotional and social withdrawal, poverty of speech) are prominent.

Risperidone Tablets also alleviate affective symptoms (such as depression, guilt feelings, anxiety) associated with schizophrenia.

Risperidone Tablets are also effective in maintaining the clinical improvement during continuation therapy in patients who have shown an initial treatment response.

They are also indicated for the treatment of mania in bipolar disorder. These episodes are characterized by symptoms such as elevated, expansive or irritable mood, inflated self-esteem, decreased need for sleep, pressured speech, racing thoughts, distractibility, or poor judgment, including disruptive or aggressive behaviours.

Risperidone Tablets are not licensed for the treatment of behavioural symptoms of dementia.

These applications for Risperidone were submitted at the same time. The bioequivalence study was sufficient to confirm the bioequivalence of the product to the reference product.
PHARMACEUTICAL ASSESSMENT

DRUG SUBSTANCE

INN: Risperidone
Chemical name: 4-[2-[4-(6-fluorobenzo[d]isoxazol-3-yl)-1-piperidyl]ethyl]-3-methyl-2,6-diazabicyclo[4.4.0]deca-1,3-dien-5-one

Structure:

CAS registry number: 106266-06-2
Physical form: White to off-white powder, practically insoluble in water, freely soluble in methylene chloride, and sparingly soluble in alcohol. It dissolves in dilute acid solutions.

Molecular formula: C_{23}H_{27}FN_{4}O_{2}
Molecular weight: 410.5

Risperidone is the subject of a European Pharmacopoeia monograph.

Synthesis of the drug substance from the designated starting material has been adequately described and appropriate in-process controls and intermediate specifications are applied. Satisfactory specification tests are in place for all starting materials and reagents and these are supported by relevant certificates of analysis. No materials of animal or human origin are used in the production of the active substance.

An appropriate specification based on the European Pharmacopoeia has been provided.

Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications.

All potential known impurities have been identified and characterised.

Active risperidone is stored in appropriate packaging. The specifications and typical analytical test reports are provided and are satisfactory.

Batch analysis data are provided and comply with the proposed specification.

Satisfactory certificates of analysis have been provided for working standards used by the active substance manufacturer and finished product manufacturer during validation studies.

Appropriate stability data have been generated, supporting the retest period for the active substance.
DRUG PRODUCT

Other ingredients
Other ingredients consist of pharmaceutical excipients, namely lactose monohydrate, maize starch, microcrystalline cellulose, povidone, magnesium stearate, colloidal anhydrous silica, sodium laurilsulfate, carnauba wax, OPADRY red (0.5mg) and OPADRY white (1mg, 2mg, 3mg, 4mg, and 6mg).

All excipients used comply with their respective European Pharmacopoeial monograph, with the exception of OPADRY red and OPADRY white which comply with in-House specifications.

Satisfactory specifications and Certificates of Analysis have been provided for all excipients.

The only excipient used that contains material of animal or human origin is lactose monohydrate. The application has provided a declaration that milk used in the production of lactose monohydrate is sourced from healthy animals under the same conditions as that for human consumption.

Dissolution and Impurity profiles
Dissolution and impurity profiles for all strengths of the drug product were found to be generic medicinal products equivalent to those of the reference products.

Manufacture
A description and flow-chart of the manufacturing method have been provided.

In-process controls are appropriate considering the nature of the product and the method of manufacture. Process validation has been carried out on batches of each strength. The results are satisfactory.

Finished product specification
The finished product specification is satisfactory. Acceptance limits have been justified with respect to conventional pharmaceutical requirements and, where appropriate, safety. Test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Certificates of analysis have been provided for any working standards used.

Container Closure System
The product is packaged in PVDC-coated PVC blisters, sealed with aluminium foil with package sizes of 20, 28, 56 and 60 tablets per box. Specifications and Certificates of Analysis for all packaging used have been provided. This is satisfactory. All primary product packaging complies with EU legislation regarding contact with food.

Not all pack sizes are to be marketed. However, the Marketing Authorisation Holder has committed to submitting mock-ups to the regulatory authorities for approval before marketing any pack size.
Stability
Finished product stability studies have been conducted in accordance with current guidelines. Based on the results, a shelf-life of 2 years with storage condition ‘Store below 30 degree C’ is proposed which is satisfactory.

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

The requirements for essential similarity of the proposed and reference products have been met with respect to qualitative and quantitative content of the active substance, pharmaceutical form and bioequivalence.
PRECLINICAL ASSESSMENT

No new preclinical data have been supplied with these applications and none are required for an application of this type.
CLINICAL ASSESSMENT

1. INTRODUCTION
These are national abridged applications claiming essential similarity to Risperdal Tablets (Jansen Cilag) PL 00242/0347, which has been licensed in the UK for more than 10 years.

2. BACKGROUND
Risperidone is well characterised in the literature and is indicated for the treatment of acute and chronic schizophrenic psychoses. It belongs to a new class of antipsychotic agents, the benzisoxazole-derivatives.

Risperidone is a selective monoaminergic antagonist with a high affinity for both serotonergic 5-HT2 and dopaminergic D2 receptors. It binds also to alpha1-adrenergic receptors and, with lower affinity, to H1-histaminergic and alpha2-adrenergic receptors. It has no affinity for cholinergic receptors. Although Risperidone is a potent D2 antagonist, which is considered to be the principal mechanism by which it improves the positive symptoms of schizophrenia, it causes less depression of motor activity and induction of catalepsy than classical neuroleptics. Balanced central serotonin and dopamine antagonism may reduce the tendency to cause extrapyramidal side effects, and extend the therapeutic activity to the negative and affective symptoms of schizophrenia.

3. INDICATIONS
Risperidone Tablets are indicated for the treatment of acute and chronic schizophrenic psychoses and other psychotic conditions in which positive symptoms (such as hallucinations, delusions, thought disturbances, hostility, suspiciousness), and/or negative symptoms (such as blunted affect, emotional and social withdrawal, poverty of speech) are prominent. Risperidone Tablets also alleviate affective symptoms (such as depression, guilt feelings, anxiety) associated with schizophrenia.

Risperidone Tablets are also effective in maintaining the clinical improvement during continuation therapy in patients who have shown an initial treatment response.

Risperidone Tablets are indicated for the treatment of mania in bipolar disorder. These episodes are characterized by symptoms such as elevated, expansive or irritable mood, inflated self-esteem, decreased need for sleep, pressured speech, racing thoughts, distractibility, or poor judgment, including disruptive or aggressive behaviours.

Risperidone Tablets are not licensed for the treatment of behavioural symptoms of dementia

4. DOSE & DOSE SCHEDULE
4.2. a Schizophrenia:
Switching from other antipsychotics: where medically appropriate, gradual discontinuation of the previous treatment while Risperidone Tablets therapy is initiated is recommended. Where medically appropriate when switching patients from depot antipsychotics, consider initiating Risperidone Tablets therapy in place of the
next scheduled injection. The need for continuing existing antiparkinson medication should be re-evaluated periodically.

Adults
Risperidone Tablets may be given once or twice daily. All patients, whether acute or chronic, should start with 2 mg/day Risperidone Tablets. The dosage may be increased to 4 mg/day on the second day. Some patients, such as first episode patients, may benefit from a slower rate of titration. From then on the dosage can be maintained unchanged, or further individualised, if needed. Most patients will benefit from daily doses between 4 and 6 mg/day although in some, an optimal response may be obtained at lower doses.

Doses above 10 mg/day generally have not been shown to provide additional efficacy to lower doses and may increase the risk of extrapyramidal symptoms. Doses above 10 mg/day should only be used in individual patients if the benefit is considered to outweigh the risk. Doses above 16 mg/day have not been extensively evaluated for safety and therefore should not be used.

Elderly
A starting dose of 0.5 mg bd is recommended. This dosage can be individually adjusted with 0.5 mg bd increments to 1 to 2 mg bd.

Children
Use of Risperidone Tablets for schizophrenia in children aged less than 15 years has not been formally evaluated.

Renal and liver disease
A starting dose of 0.5 mg bd is recommended. This dosage can be individually adjusted with 0.5 mg bd increments to 1 to 2 mg bd.

Risperidone Tablets should be used with caution in this group of patients until further experience is gained.

4.2. b Bipolar Mania:
Adults
Risperidone should be administered on a once daily schedule, starting with 2 mg. Dosage adjustments, if indicated, should occur at intervals of not less than 24 hours and in dosage increments of 1 mg per day. A dosing range between 1 and 6 mg per day is recommended.
As with all symptomatic treatments, the continued use of Risperidone Tablets must be evaluated and justified on an ongoing basis.

Elderly
A starting dose of 0.5 mg bd is recommended. This dosage can be individually adjusted with 0.5 mg bd increments to 1 to 2 mg bd.

Renal and liver disease
A starting dose of 0.5 mg bd is recommended. This dosage can be individually adjusted with 0.5 mg bd increments to 1 to 2 mg bd.
Risperidone Tablets should be used with caution in this group of patients until further experience is gained.

Combined use with mood stabilisers
There is limited information on the combined use of Risperidone Tablets with carbamazepine in bipolar mania. Carbamazepine has been shown to induce the metabolism of risperidone producing lower plasma levels of the antipsychotic fraction of Risperidone Tablets (see Section 4.5 Interaction with other medicinal products and other forms of interaction). It is therefore not recommended to co-administer Risperidone Tablets with carbamazepine in bipolar mania patients until further experience is gained. The combined use with lithium or valproate does not require any adjustment of the dose of Risperidone Tablets.

Method of administration
Oral use.

5. TOXICOLOGY
No new data.

6. CLINICAL PHARMACOLOGY
Risperidone is extensively metabolized in the liver by cytochrome P450 2D6 to a major active metabolite, 9-hydroxyrisperidone, which appears approximately equipotent with risperidone, with respect to receptor binding activity. Consequently, the clinical effect of the drug likely results from the active moiety (the combined concentrations of risperidone plus 9-hydroxyrisperidone). The hydroxylation of risperidone, and hence the concentrations of parent drug and active metabolite, differ substantially in extensive and poor CYP2D6 metabolizers. However, the concentration of the active moiety did not differ substantially between extensive and poor metabolizers, and elimination half-lives were similar in all subjects (20 to 24 hours).

The kinetics of the individual components of the active moiety, risperidone and its 9-hydroxy metabolite, are both dose proportional after doses of risperidone up to 25mg daily. Mean peak plasma concentrations of risperidone and 9-hydroxyrisperidone were reached at about 1 hour and 3 hours, respectively, after drug administration. Food did not affect the extent of absorption.

Bioequivalence study
Test product: Risperidone 1mg tablets
Reference product: Risperdal 1mg tablets

A single open label, randomised, two treatment, two period, cross-over, single-dose bioequivalence study is presented in support of this application, comparing risperidone 1mg Tablets of Dexcel Ltd., Israel and Risperdal 1mg Tablets of Janssen Cilag Ltd, UK. Healthy adult male and female subjects (including two alternates) were dosed under fasting conditions. The protocol is satisfactory. Sampling schedules were satisfactory for accurate determination of AUC_T, AUC_{inf} and Cmax.
It is conventional in bioequivalence testing to test the highest dosage form in comparative bioavailability studies and extrapolate from those results to bioequivalence of the lower dosage forms. In this case a low dosage has been tested. The applicant provided an acceptable justification, on ethical and safety grounds, for the use of a low dose in the bioequivalence study.

### Descriptive Statistics for Pharmacokinetic Parameters of Risperidone

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<tr>
<th></th>
<th>C&lt;sub&gt;max&lt;/sub&gt; (pg/mL)</th>
<th>AUC&lt;sub&gt;T&lt;/sub&gt; (pg*h/mL)</th>
<th>AUC&lt;sub&gt;inf&lt;/sub&gt; (pg*h/mL)</th>
<th>T&lt;sub&gt;max&lt;/sub&gt; (h)</th>
<th>t&lt;sub&gt;1/2&lt;/sub&gt; (h)</th>
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<td>Test</td>
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<tr>
<td>Reference</td>
<td>Mean&lt;sup&gt;a&lt;/sup&gt;</td>
<td>6335.8</td>
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<td>Treatment effect p-value&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.0512</td>
<td>0.0484</td>
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<td>0.9288</td>
<td>0.1192</td>
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<td>Ratio of Test/Reference&lt;sup&gt;c&lt;/sup&gt;</td>
<td>108.5</td>
<td>112.3</td>
<td>112.4</td>
<td>100.7</td>
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<td>90% CI of ratio&lt;sup&gt;d&lt;/sup&gt;</td>
<td>101.36–116.13</td>
<td>102.06–123.48</td>
<td>102.2–123.62</td>
<td>95.57–119.41&lt;sup&gt;f&lt;/sup&gt;</td>
<td>99.36–122.35</td>
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</table>

<sup>a</sup> Arithmetic mean  
<sup>b</sup> Based on data transformed to natural logarithm (except T<sub>max</sub> and t<sub>1/2</sub>).  
<sup>c</sup> Median  
<sup>d</sup> Range  
<sup>e</sup> Non-parametric confidence interval  

### Descriptive Statistics for Pharmacokinetic Parameters of 9-Hydroxy-Risperidone

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<th>t&lt;sub&gt;1/2&lt;/sub&gt; (h)</th>
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<td>Reference</td>
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<td>Treatment effect p-value&lt;sup&gt;b&lt;/sup&gt;</td>
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<td>90% CI of ratio&lt;sup&gt;d&lt;/sup&gt;</td>
<td>94.81–108.17</td>
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<td>96.48–106.60</td>
<td>105.87–161.41&lt;sup&gt;f&lt;/sup&gt;</td>
<td>94.66–113.16</td>
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</table>

<sup>a</sup> Arithmetic mean  
<sup>b</sup> Based on data transformed to natural logarithm (except T<sub>max</sub> and t<sub>1/2</sub>).  
<sup>c</sup> Median  
<sup>d</sup> Range  
<sup>e</sup> Non-parametric confidence interval

The 90% confidence intervals of AUC<sub>T</sub> and AUC<sub>inf</sub> for risperidone were only just contained in the acceptable range of 80 to 125%, with a point estimate of 12% supra-availability of the test product. In contrast however the AUC ratios for 9-hydroxy-risperidone were close to unity. Some non-linearity of conversion to the active metabolite could be an explanation or there might be no true difference between the parent drug and metabolite as the confidence intervals overlap considerably.
In any event all of the key 90% confidence intervals were completely contained in the acceptable range of 80 to 125% and it is concluded that bioequivalence in accordance with standard criteria has been shown.

Bioequivalence has been demonstrated between the applicant’s Risperidone 1mg Film-Coated Tablets and the reference product Risperdal 1mg Tablets (Janssen-Cilag Limited, UK). As these products meet all the criteria as specified in the Note for Guidance on the investigation of bioavailability and bioequivalence (CPMP/EWP/QWP/1401/98), the results and conclusions of the bioequivalence study on the 1mg strength can be extrapolated to the 0.5, 2, 3, 4 and 6mg strength tablets.

7. **Efficacy**
No new data.

8. **Safety**
No new data.

9. **Expert Reports**
A satisfactory expert report is provided by an appropriately qualified physician.

10. **Patient Information Leaflet (PIL)**
This is satisfactory.

11. **Labelling**
Full colour mock-ups are provided. The labelling is medically satisfactory.

12. **Application Form (MAA)**
The MAAs are medically satisfactory.

13. **Summary of Product Characteristics (SPC)**
The SPC is essentially identical to the current approved SPC for the reference product and is satisfactory.

14. **Discussion**
The requested indications and other SPC details are consistent with current originator SPC. Bioequivalence to the reference product is established.

15. **Medical Conclusion**
Marketing Authorisations may be granted for these preparations.
OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY
The important quality characteristics of Risperidone 0.5mg, 1mg, 2mg, 3mg, 4mg, and 6mg Film-Coated Tablets 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.

PRECLINICAL
No new preclinical data were submitted and none are required for applications of this type.

EFFICACY
A bioequivalence study was carried out and the test and reference products shown to be bioequivalent for the appropriate pharmacokinetic criteria.

No new or unexpected safety concerns arise from these applications.

The SPC and PIL are satisfactory and consistent with that for the UK reference products.

RISK BENEFIT ASSESSMENT
The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The bioequivalence study supports the claim that the applicant’s product and the reference product are interchangeable. Extensive clinical experience with risperidone is considered to have demonstrated the therapeutic value of the compound. The risk benefit is therefore considered to be positive.
RISPERIDONE 0.5MG FILM-COATED TABLETS
RISPERIDONE 1MG FILM-COATED TABLETS
RISPERIDONE 2MG FILM-COATED TABLETS
RISPERIDONE 3MG FILM-COATED TABLETS
RISPERIDONE 4MG FILM-COATED TABLETS
RISPERIDONE 6MG FILM-COATED TABLETS

PL 14017/0130-5

**STEPS TAKEN FOR ASSESSMENT**

<p>| | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>1</td>
<td>The MHRA received the marketing authorisation applications on 26th July 2005</td>
</tr>
<tr>
<td>2</td>
<td>Following standard checks and communication with the applicant the MHRA considered the application valid on 19th September 2005</td>
</tr>
<tr>
<td>3</td>
<td>Following assessment of the application the MHRA requested further information relating to the clinical dossier on 19th July 2006 and quality dossiers on 12th January 2006, 9th October 2006, and 23rd May 2007</td>
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<tr>
<td>4</td>
<td>The applicant responded to the MHRA’s requests, providing further information on clinical dossier on the 28th September 2006 and quality dossier on 22nd October 2006, 23rd March 2007 and 14th June 2007</td>
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<td>5</td>
<td>The application was determined on 16th October 2007</td>
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RISPERIDONE 0.5MG FILM-COATED TABLETS
RISPERIDONE 1MG FILM-COATED TABLETS
RISPERIDONE 2MG FILM-COATED TABLETS
RISPERIDONE 3MG FILM-COATED TABLETS
RISPERIDONE 4MG FILM-COATED TABLETS
RISPERIDONE 6MG FILM-COATED TABLETS

PL 14017/0130-5

STEPS TAKEN AFTER ASSESSMENT

A list of major non-safety variations of clinical interest granted are presented below:

<table>
<thead>
<tr>
<th>Date submitted</th>
<th>Application type</th>
<th>Scope</th>
<th>Outcome</th>
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<tr>
<td>30/06/2012</td>
<td>IB</td>
<td>To update sections 4.4, 4.6 and 4.8 of the SmPC to bring in line with the brand leader Risperdal (Janssen-Cilag Ltd). Consequentially the PIL has also been updated.</td>
<td>Granted 11/09/2012</td>
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<td>02/07/2013</td>
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<td>To update sections 4.4, 4.5 and 4.6 of the SmPC to bring in line with the brand leader Risperdal (Janssen-Cilag Ltd). Consequentially the PIL has also been updated.</td>
<td>Granted 31/07/2013</td>
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</table>
SUMMARY OF PRODUCT CHARACTERISTICS
The current approved UK versions of the Summaries of Product Characteristics (SmPCs) for these products are available on the MHRA website.

PATIENT INFORMATION LEAFLET
The current approved UK versions of the Patient Information Leaflets (PILs) for these products are available on the MHRA website.

LABELLING
<table>
<thead>
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<th>Dose</th>
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<td>0.5mg</td>
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<td>6mg</td>
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PL 140700302

Each film-coated tablet contains risperidone 2 mg.
Also contains lactose. See package leaflet for further information. For oral use.

Dosage: as directed by the physician.

Please read the package leaflet before use.

Do not store above 30°C.

Keep out of the sight and reach of children.

Risperidone 2mg Film-Coated Tablets

MARKETING AUTHORIZATION HOLDER:
Dexcel Pharma Ltd,
7 Sovereign Way, Duxford Fields, Duxford,
Cambridgeshire, CB22 4PS, UK

Risperidone 0.5, 1, 2, 3, 4 and 6mg Film-Coated Tablets

PL 14017/0130-5
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Annex 1

Reference: PL 14017/0130-0024; PL 14017/0131-0026; PL 14017/0132-0022; PL 14017/0133-0024; PL 14017/0134-0024; PL 14017/0135-0024

Product: Risperidone 0.5 mg, 1 mg, 2 mg, 3 mg, 4 mg and 6 mg Film-Coated Tablets

Marketing Authorisation Holder: Dexcel Pharma Limited

Active Ingredient(s): Risperidone

Reason:
To update sections 4.4, 4.6 and 4.8 of the SmPC to bring in line with the brand leader Risperdal (Janssen-Cilag Ltd). Consequentially, the PIL has also been updated.

Supporting Evidence
A revised PIL and SmPC have been provided. The currently approved labelling is acceptable and needs no further revisions.

Evaluation
The amended sections of the SmPC and the amended PIL are satisfactory.

The current approved UK versions of the Summaries of Product Characteristics (SmPCs) and Patient Information Leaflets (PILs) for these products are available on the MHRA website.

Decision
Approved on 11 September 2012.
Annex 2

Reference: PL 14017/0130-0028; PL 14017/0131-0031; PL 14017/0132-0027; PL 14017/0133-0029; PL 14017/0134-0029; PL 14017/0135-0029

Product: Risperidone 0.5mg, 1mg, 2mg, 3mg, 4mg and 6mg Film-Coated Tablets

Marketing Authorisation Holder: Dexcel Pharma Limited

Active Ingredient(s): Risperidone

Reason:
To update sections 4.4, 4.5 and 4.6 of the SmPC to bring in line with the brand leader Risperdal (Janssen-Cilag Ltd). Consequentially, the PIL has also been updated.

Supporting Evidence
A revised PIL and SmPC have been provided. The currently approved labelling is acceptable and needs no further revisions.

Evaluation
The amended sections of the SmPC and the amended PIL are satisfactory.

The current approved UK versions of the Summaries of Product Characteristics (SmPCs) and Patient Information Leaflets (PILs) for these products are available on the MHRA website.

Decision
Approved on 31 July 2013.