Abstract:
The present invention relates to a prolonged release dosage form comprising amisulpride preferably in the form of a multunit pellets or micro tablets filled into capsule or compressed in to tablet or bilayered tablet. It also relates to the process for preparing the said dosage form.
PROLONGED RELEASE FORMULATION OF AMISULPRIDE

FIELD OF THE INVENTION

The present invention relates to a prolonged release dosage form comprising amisulpride preferably in the form of a multiunit pellets or micro tablets filled into capsule or compressed in to tablet or bilayered tablet. It also relates to the process for preparing the said dosage form.

BACKGROUND OF THE INVENTION

Amisulpride is a selective dopamine antagonist used in the treatment of psychoses, more particularly in the treatment of paranoid and productive schizophrenia or acute delirious psychoses and in the treatment of schizophrenia deficiency states, residual psychotic changes and inhibitory states with slowing. It is commercially available in the dosage range from 50 mg to 400 mg as immediate release tablets in the trade name of Solian® Tablets. Amisulpride shows linear pharmacokinetics with bioavailability of 48%, low protein binding (17%) and an elimination half-life of -12 h. It is predominantly eliminated in the urine as the parent compound. Its dosage ranges from 200 to 1200 mg/day. Hence patients would be required to take several tablets daily, which results in patient incompliance.

Therefore, it would be of considerable clinical benefit to design orally deliverable dosage form of amisulpride as a prolonged release dosage form.

Further, the administration of amisulpride by the oral route can lead to a low and/or irregular bioavailability. The term "bioavailability" is understood here as meaning the fraction of active principle which is absorbed from its pharmaceutical form and which reaches the plasma.

The low or irregular bioavailability can be the outcome of several factors amongst which are discussed below: low solubility or a very slow dissolution of the active agent; instability of
the active agent, either over the entire length of the gastrointestinal tract, or in one part of it
only; enzymatic degradation in the mucous membrane or at the hepatic level of the active
agent; slow or incomplete absorption of the active agent due to a slow passive diffusion
through the intestine, or, in the case of an active mechanism, a saturation of the transport
system.

It is known that the bioavailability of certain active agents can be modified by means of a
prolonged release formulation which releases the active agent over the entire length of the
gastrointestinal tract.

French patent 7801632 discloses the compound amisulpride, its isomers and some of its
derivatives.

US6069165 discloses a pharmaceutical composition of amisulpride comprising of a
lipophilic phase. The lipid materials that can be used in the present invention may be one or
more of fatty acids, glycerides, mineral oils or other oils. It claims to increase the
bioavailability of the drug by incorporating the lipid phase in the dosage form.

JP62178518 discloses a once a day formulation of a sulpiride. The dosage form comprises of
more than two hydrogel forming excipients like gelatin, hydroxypropyl cellulose,
methylcellulose, etc. It discloses the use of mixtures of water and ethanol for the granulation
of the active compound with that of the hydrogel forming excipients.

US20010046473 discloses a gastric retained dosage form of amisulpride comprising of
carbon dioxide gas generating system and a polymeric composition capable of retaining the
generated gas. So it provides a floating dosage form of amisulpride. According to applicant
benzamides, such as amisulpride are generally poorly absorbed at the colonic level in man,
but that, on the other hand, they are better absorbed in the small intestine. For certain of these
benzamides, absorption takes place quasi-exclusively in the upper parts of the small intestine, that is to say the jejunum, the duodenum or the proximal ileum. Hence, applicant has considered improving the bioavailability of the amisulpride by formulating them in the form of a pharmaceutical composition for gastric residence favouring absorption at the level of the small intestine, or even, more specifically, the upper parts of the small intestine. However, there are some disadvantages associated with gastroretentive system, like the tablet may get stuck in the pylorus; variability in bioavailability, depending on standing or sleeping position of patient.

US6861072 discloses a controlled release gastric retained dosage form of an active agent covering amisulpride. The dosage form of the invention comprises a gas generating system, hydrophilic polymer matrix and an excipient which is capable of modifying the release profile of the active agent.

US2006153925 A1 discloses an orodispersible dosage form of amisulpride comprising of coated particles of the drug along with excipients used conventionally in the preparation of rapidly disintegrating dosage forms. It affords immediate release of the drug.

Hence there is a need for the further development of prolonged release dosage form of amisulpride that is simple and easy to manufacture, provide better clinical effects and improved patient compliance.

**SUMMARY OF THE INVENTION**

One general embodiment of the present invention is to provide a prolonged release dosage form of amisulpride.

In yet another embodiment, the present invention provides a prolonged release dosage form of amisulpride that can be administered orally once or twice daily.
Another embodiment of the present invention is to provide a prolonged release dosage form of amisulpride in the form of a bilayer tablet comprising of a prolonged release blend and an immediate release blend.

Another embodiment of the present invention is to provide a method of preparation of a prolonged release dosage form of amisulpride, which comprises of two parts, wherein the first part is immediate release part which is manufactured by mixing amisulpride with suitable diluent and optionally disintegrant, then granulating with a binder solution and drying the granules, The dried granules being milled or suitably size reduced and mixed with lubricants and optionally with other pharmaceutically acceptable ingredients; the second part being the prolonged release part is manufactured by mixing amisulpride with suitable diluent, release controlling agent and optionally other pharmaceutically acceptable excipient and granulating with a binder solution and drying the granules, the dried granules being milled or suitably size reduced and mixed with lubricants and optionally with other pharmaceutically acceptable ingredients; the said parts of amisulpride being formulated into a suitable dosage form.

In yet another embodiment, the present invention provides a prolonged release dosage form of amisulpride in monolithic form.

Another embodiment of the present invention is to provide a method of preparation of a prolonged release dosage form of amisulpride in monolithic form by mixing amisulpride with suitable diluent, release controlling agent(s) and optionally other pharmaceutically acceptable excipient and granulating with a binder solution and drying the granules, the dried granules being milled or suitably size reduced and mixed with lubricants and optionally with other pharmaceutically acceptable ingredients.
In yet another embodiment, the present invention provides a prolonged release dosage form of amisulpride in multiunit pellets, adapted to be formulated in a capsule or compressed in a tablet.

Yet another aspect of the present invention is to provide a method of treating a mammal, particularly a human being in need thereof, comprising administering the said dosage form.

DETAILED DESCRIPTION

The use of the terms "a" and "an" and "the" and similar referents in the context of describing the invention (are to be construed to cover both the singular and the plural, unless otherwise indicated herein or clearly contradicted by context.

In one general embodiment, the present invention provides prolonged release dosage form of amisulpride, more particularly a bilayer tablet of amisulpride which comprises of: a) Immediate release blend and b) Prolonged release blend.

The term "dosage form" or "composition" denotes any physical form of the formulation that contains an amount sufficient to produce a therapeutic effect with a single administration. It may be in the form of solid dosage form like tablets, capsules etc. The preferred dosage form of the present invention is a tablet like multilayered tablets, monolithic tablets, compression coated tablets or inlay tablets. The most preferred dosage form is a bilayer tablet.

The term "immediate release blend" or "immediate release part" as used herein or elsewhere encompasses mixtures of excipients and active agent which provide immediate release of the active agent when administered to a patient. It can be clear to a person of ordinary skill that immediate release blend can be prepared by dry granulation process or by wet granulation process or by direct compression process. The preferred process is a wet granulation process.
The term "prolonged release blend" or "prolonged release part" as used herein or elsewhere encompass mixtures of active agent, rate controlling polymer(s) and pharmaceutically acceptable excipients. The term "prolonged release" can be conveniently replaced by similar terms like modified release, controlled release, timed release, retarded release, extended release and delayed release, etc. The prolonged release blend of the present invention can be prepared by conventional methods like polymer matrix composition, coating composition or likewise. "Prolonged release" is defined herein as release of an active agent in a continuous manner over a prolonged period of time. By "prolonged period of time" it is meant a continuous period of time of greater than about 1 hour, preferably, greater than about 4 hours, more preferably, greater than about 8 hours.

For the bilayered tablet composition, 20-30% w/w, preferably 25-28% w/w of active agent is used in immediate release part and 80 to 70% w/w, preferably 75 to 72% w/w of active agent is used in prolonged release part.

According to instant invention, the desired release profile of Amisulpride is as below:
1 hour - Not more than 50%
4 hour - Not more than 85%
8 hour - More than 90%

The dissolution condition being:

Apparatus: USP Type II (Paddle); RPM: 50
0 - 2hr, 900 mL, 0.01 N HCl followed by
2 - 3hr, 900 mL, 4.5 pH Acetate buffer followed by
3 - 8 hr, 900 mL, 6.8 pH Phosphate buffer
The term "amisulpride" or "drug" or "active agent" as used herein is to encompass free base, metabolites, optically active enantiomer or pharmaceutically acceptable acid addition salts or mixtures thereof. It is also intended to include various polymorphic forms of amisulpride or its pharmaceutically acceptable acid addition salts. The quantity of the amisulpride in the dosage form can be between 10 mg to 1000 mg, preferably 50 mg to 500 mg.

In another embodiment, in the present invention the particle size of 90% particles ($D_{90}$) of amisulpride are less than 50 microns; preferably less than 30 microns; more preferably less than 20 microns; & most preferably less than 10 microns and the 50% particles ($D_{50}$) are less than 10 microns.

According to instant invention, the most preferred particle size of amisulpride is as follows:

A. Particle size of 90% particles of amisulpride is less than 30 microns.

A. Particle size of 50% particles of amisulpride is less than 10 microns.

The formulation can be made into capsule or a bilayered tablet, tablet in a tablet, inlay tablet or mini-tablets filled in a capsule and other dosage form.

For the monolithic form granules can be formulated into a capsule or compressed into tablet.

The excipients that can be used as the release controlling agent within the granule(s) and over the tablet as coating are described in greater detail herein below.

The release controlling agents as used herein in the granulation or coating are selected from pH independent polymer and pH dependent polymer more preferably pH independent polymer. The release controlling agent may be hydrophillic or hydrophobic in nature.
The pH dependent polymer that can be employed in the present invention may be such as, for example, an alginate material, a carboxyvinyl polymer or a sodium salt of carboxymethyl cellulose.

The pH independent release controlling polymer may be selected from the group comprising of hydroxy propyl methyl cellulose, hydroxy propyl ethyl cellulose, hydroxy propyl cellulose, hydroxy ethyl cellulose, methyl cellulose, xantham gum or polyethylene oxide, ammonio methacrylate copolymers type A and B as described in USP, polyacrylate dispersion 30% as described in Ph. Eur., or combination thereof.

The preferred release controlling agent of the present invention is hydroxy propyl methyl cellulose sold under the brand name of Hypromellose.

The combination of hydrophillic polymer like low viscosity hypromellose and disintegrants-like crospovidone are used in instant invention to achieve desired prolonged release profile, wherein hydrophillic polymer will act as matrix to retard the dissolution of active agent and disintegrant will absorb water which will cause faster hydration of the hydrophillic matrix.

A dosage form as described herein may comprise one or more pharmaceutically acceptable excipients, during granulation, compression or coating, and may be selected from diluent/filler, glidants, disintegrant, binder, lubricant, release controlling agents, plasticizers, opacifiers, stabilizers, anti-tacking agent, surfactant, coloring agent and others known to the skilled person in the art. As will be appreciated by those skilled in the art, the exact choice of excipient and their relative amounts will depend to some extent on the final oral dosage form.

Examples of "diluents" or "fillers" include but not limited to dibasic calcium phosphate, lactose anhydrous, lactose monohydrate, pregelatinized starch, mannitol, microcrystalline
cellulose, powdered cellulose, sorbitol, starch or mixtures thereof. The diluent may be present in an amount ranging from 1% to 80% by weight of the composition.

Examples of "binders" include but not limited to polyvinylpyrrolidone, copovidone, cellulose derivatives, shellac, zein, gelatin, polymethacrylates, synthetic resins, acrylates or mixtures thereof. The binder may be present in an amount ranging from 0.1% to 10% by weight of the composition.

Examples of "glidants" or "anti-tacking agents" include but not limited to colloidal silica, talc, calcium silicate, magnesium silicate, colloidal silicon dioxide or mixtures thereof. The glidant or anti-tacking agent may be present in an amount ranging from 0.1% to 5% by weight of the composition.

Examples of "lubricants" include but not limited to Stearic acid, Polyethylene glycol, Magnesium stearate, Calcium stearate, Zinc stearate, Talc or Silica, Hydrogenated castor oil or mixtures thereof. The lubricant may be present in an amount ranging from 0.1% to 5% by weight of the composition.

Examples of "surfactants" include but not limited to sodium dodecyl sulfate, ammonium lauryl sulfate, and other alkyl sulfate, dodecyl betaine, dodecyl dimethylamine oxide, alkyl poly (ethylene oxide), copolymers of poly (ethylene oxide) and poly (propylene oxide) commercially called as poloxamers. The preferred surfactants are inhibitor of the P-glycoprotein like polyethoxylated tocopheryl succinate, polyoxyethylene castor oil or polyethoxylated castor oil, polyoxyethylene sorbitan monolaurate (Tween®20), polyoxyethylene sorbitan monopalmitate (Tween®40), polyoxyethylene sorbitan monostearate (Tween®60), polyoxyethylene sorbitan monooleate (Tween®80), polyethylene glycol monostearate (Polyoxyl 40 stearate), polyoxyethylene-polyoxypropylene copolymers, octylphenolethoxylate, etc.
The most preferable surfactant in the present invention is polyethylene glycol monostearate (Polyoxyl 40 Stearate). The surfactant may be present preferably in the range of 0.25-5%.

Plasticizer may be used in a coat to increase the flexibility and strength of the layer and may be selected from Triethyl citrate, PEG 6000, Glyceryl monopalmotostearate / Glyceryl monostearate, Dibutyl phthalate, Macrogol or other materials known to one of ordinary skill in the art.

Examples of opacifier includes but not limited to titanium dioxide or talc.

Examples of solvents used to prepare solution of release controlling agent for the granulation or coating includes aqueous or organic solvent or combination thereof.

The immediate release blend or prolonged release blend of the present invention can be prepared by any method known to the person skilled in art such as wet granulation, direct compression, extrusion spheronization or any other possible methods. Preferably wet granulation method is applied.

In another general embodiment, the present invention provides process for preparing the prolonged release dosage form according to present invention.

The general manufacturing process is as below:

The pharmaceutical composition is prepared in two parts. The first part is immediate release part which is manufactured by mixing Amisulpride with suitable diluent and optionally disintegrant, then granulating with a binder solution and drying the granules. The dried granules may be milled or suitably size reduced and mixed with lubricants and optionally with other pharmaceutically acceptable ingredients.
The second part is prolonged release part which is manufactured by mixing Amisulpride with suitable diluent, release controlling agent(s) and optionally other pharmaceutically acceptable excipient and granulating with a binder solution and drying the granules. The dried granules may be milled or suitably size reduced and mixed with lubricant and optionally with other pharmaceutically acceptable ingredients.

The above said parts of amisulpride may be formulated into a suitable dosage form. For example, they can be formulated into a capsule or as bilayered tablet, tablet in a tablet, inlay tablet and the like.

In another embodiment, the immediate release pharmaceutical composition of amisulpride is coated over prolonged release pharmaceutical composition of amisulpride.

In another embodiment, the immediate release pharmaceutical composition of amisulpride and prolonged release pharmaceutical composition of amisulpride is filled into capsules in the form of granules, beads, pellets and the like.

In another embodiment, the prolonged release pharmaceutical dosage form of amisulpride is manufactured as single layer tablet dosage form or monolithic tablet dosage form.

The invention will be further illustrated by the following Examples, however, without restricting its scope to these embodiments.
EXAMPLE-I

Table I

<table>
<thead>
<tr>
<th>Sr. No</th>
<th>Ingredients</th>
<th>Mg/Tab</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Immediate release (IR) blend</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Dry mix</strong></td>
<td></td>
</tr>
<tr>
<td>1.</td>
<td>Amisulpride</td>
<td>112.00</td>
</tr>
<tr>
<td>2.</td>
<td>Lactose Monohydrate</td>
<td>54.60</td>
</tr>
<tr>
<td>3.</td>
<td>Microcrystalline Cellulose</td>
<td>54.26</td>
</tr>
<tr>
<td>4.</td>
<td>Colloidal Silicon Dioxide</td>
<td>5.25</td>
</tr>
<tr>
<td>5.</td>
<td>Ferric oxide red</td>
<td>0.90</td>
</tr>
<tr>
<td></td>
<td><strong>Granulation</strong></td>
<td></td>
</tr>
<tr>
<td>1.</td>
<td>Polyoxyl 40 Stearate</td>
<td>1.75</td>
</tr>
<tr>
<td>2.</td>
<td>Hydroxy propyl methyl cellulose</td>
<td>10.29</td>
</tr>
<tr>
<td>3.</td>
<td>Purified Water*</td>
<td>q.s.</td>
</tr>
<tr>
<td></td>
<td><strong>Blending</strong></td>
<td></td>
</tr>
<tr>
<td>1.</td>
<td>Sodium Starch Glycolate</td>
<td>25.05</td>
</tr>
<tr>
<td>2.</td>
<td>Microcrystalline cellulose (PH 200)</td>
<td>19.19</td>
</tr>
<tr>
<td>3.</td>
<td>Colloidal Silicon Dioxide</td>
<td>5.88</td>
</tr>
<tr>
<td>4.</td>
<td>Talc</td>
<td>5.88</td>
</tr>
<tr>
<td>5.</td>
<td>Magnesium Stearate</td>
<td>7.35</td>
</tr>
</tbody>
</table>

Table II

<table>
<thead>
<tr>
<th>Sr. No</th>
<th>Ingredients</th>
<th>Mg/Tab</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Prolonged Release Blend</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Dry Mix</strong></td>
<td></td>
</tr>
<tr>
<td>1.</td>
<td>Amisulpride</td>
<td>288.00</td>
</tr>
<tr>
<td>2.</td>
<td>Lactose Monohydrate</td>
<td>55.68</td>
</tr>
<tr>
<td>3.</td>
<td>Microcrystalline Cellulose</td>
<td>37.44</td>
</tr>
<tr>
<td>4.</td>
<td>Hydroxy Propyl Methyl Cellulose (K 100LV)</td>
<td>115.20</td>
</tr>
<tr>
<td>5.</td>
<td>Crospovidone</td>
<td>23.04</td>
</tr>
<tr>
<td></td>
<td><strong>Granulation</strong></td>
<td></td>
</tr>
<tr>
<td>1.</td>
<td>Hydroxy Propyl Methyl Cellulose</td>
<td>11.52</td>
</tr>
<tr>
<td>2.</td>
<td>Isopropyl Alcohol*</td>
<td>q.s.</td>
</tr>
<tr>
<td>3.</td>
<td>Water*</td>
<td>q.s.</td>
</tr>
<tr>
<td></td>
<td><strong>Blending</strong></td>
<td></td>
</tr>
<tr>
<td>1.</td>
<td>Microcrystalline Cellulose</td>
<td>28.80</td>
</tr>
<tr>
<td>2.</td>
<td>Colloidal Silicon Dioxide</td>
<td>11.52</td>
</tr>
<tr>
<td>3.</td>
<td>Magnesium Stearate</td>
<td>14.40</td>
</tr>
</tbody>
</table>
Manufacturing Process:

1) Preparation of Immediate Release (IR) Blend:

1. Amisulpride, Lactose Monohydrate, Microcrystalline Cellulose, Colloidal Silicon Dioxide and Ferric oxide red were sifted through appropriate sieves and mixed.

2. Polyoxyl 40 Stearate was mixed with some quantity of warm purified water with a stirrer. Hydroxy propyl methyl cellulose was dispersed in the remaining quantity of water with stirring till there is no lump. Then the solution of Polyoxyl 40 stearate was added in the dispersion of hydroxy propyl methyl cellulose with stirring.

3. Materials of Step No-I was loaded in RMG and granulated with the binder solution of Step No-2.

4. The wet mass obtained from the Step No- 3 was dried and sized through appropriate sieve.

5. Sodium Starch Glycolate, Microcrystalline Cellulose, Talc and Colloidal Silicon Dioxide were sifted through appropriate sieve.

6. Magnesium Stearate was sifted through appropriate sieve.

7. Granules of Step No-4 were blended with the mixtures obtained from the Step No-5 in a blender.

8. Blend of Step No-7 was lubricated with the Magnesium Stearate obtained from Step No-6 in a blender.

Preparation of Prolonged Release Blend:

1. Amisulpride, Lactose Monohydrate, Microcrystalline Cellulose, Hydroxy Propyl Methyl Cellulose (KIOOLV) and Crospovidone were sifted through appropriate sieves and mixed.
2. Hydroxy Propyl Methyl Cellulose was dispersed with the solvent mixtures of Isopropyl alcohol and water with stirring till there are no lumps.

3. Materials of Step No-I was loaded in RMG and granulated with the binder solution of Step No-2.

4. Wet mass of Step No-3 was dried and sieved through appropriate sieve.

5. Microcrystalline Cellulose and Colloidal Silicon dioxide were sifted through appropriate sieves.

6. Magnesium Stearate was sifted through appropriate sieve.

7. Granules of Step No-4 were blended with ingredients of Step No-5 in a blender.

8. Blend obtained from Step No-7 was lubricated with Magnesium Stearate of Step No-6.

Compression:

1. The IR blend and the prolonged release blend were compressed to tablets using suitable punches and compression machine.

The dissolution data of Example 1 is as below:

**Condition:**

Apparatus: USP Type II (Paddle); RPM: 50

0 - 2 hr, 900 mL, 0.01 N HCl followed by

2 - 3 hr, 900 mL, 4.5 pH Acetate buffer followed by

3 - 10 hr, 900 mL, 6.8 pH Phosphate buffer

**Result:**

<table>
<thead>
<tr>
<th>Dissolution Medium</th>
<th>Time (hrs)</th>
<th>% Drug Dissolved</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.01N HCl</td>
<td>1</td>
<td>41</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>54</td>
</tr>
<tr>
<td>pH 4.5 Acetate Buffer</td>
<td>3</td>
<td>69</td>
</tr>
<tr>
<td>pH 6.8 Phosphate Buffer</td>
<td>4</td>
<td>82</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>92</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>101</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>105</td>
</tr>
</tbody>
</table>
CLAIMS

5. A prolonged release dosage form of Amisulpride, which comprises amisulpride, release controlling agent and one or more pharmaceutically acceptable excipient.

2. The prolonged release dosage form according to claim 1, wherein the dosage form comprises of immediate release part and prolonged release part.

3. The prolonged release dosage form according to any preceding claim, wherein the dosage form is in the form of a capsule, bilayered tablet, tablet in a tablet, inlay tablet or mini-tablets filled in a capsule.

4. The prolonged release dosage form according to claim 1, wherein the dosage form is a monolithic matrix tablet.

5. The prolonged release dosage form according to any preceding claim, wherein release controlling agent is selected from the group comprising of pH independent polymer and pH dependent polymer, more preferably pH independent polymer.

6. The prolonged release dosage form according to any preceding claim, wherein the active agent is released from the dosage form in a continuous manner for a period of more than 1 hour, preferably more than 4 hours and most preferably more than 8 hours.

7. The prolonged release dosage form according to any preceding claims, wherein the dosage form comprises of Amisulpride particles having $D_{90}$ less than 50 $\mu$m, preferably less than 30 $\mu$m and $D_{50}$ less than 10 $\mu$m.

8. A process for preparing prolonged release dosage form of Amisulpride, comprising preparing an immediate release blend and prolonged release blend, which comprises: preparing immediate release blend by:
   a) Mixing Amisulpride with suitable diluent and optionally disintegrant,
   b) granulating the above blend with a binder solution and drying the granules,
c) dried granules obtained from step (b) is milled or suitably size reduced and mixed with lubricants and optionally with other pharmaceutically acceptable ingredients; and preparing prolonged release blend by:

d) mixing Amisulpride with suitable diluent, release controlling agent(s) and optionally other pharmaceutically acceptable excipients,
e) granulating the above blend with a binder solution and drying the granules,
f) dried granules obtained from step is milled or suitably size reduced and mixed with lubricants and optionally with other pharmaceutically acceptable ingredients,
g) formulating the immediate release blend and prolonged release blend into a suitable dosage form.

9. A prolonged release dosage form comprising Amisulpride as substantially herein described and illustrated with reference to the examples.