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Psychotropic Label Overview for DM

The Lilly logo is written in a black, cursive script font.

Answers That Matter.

About This Document

- This document includes commonly used antipsychotics label information in US, UK(EU), Australia, Canada and Japan
- This document is only for internal use. (e.g. senior management awareness of current antipsychotics' label content on the global markets)
- This document was based on analysis from latest PI of Apr 03
- It is understood that the accuracy of this document is limited to date of last revision

Source: Analysis from latest PI of Apr 03

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Label Version As of Nov 2002

| | Zyprexa | Risperdal | Geodon | Clozaril | Seroquel |
|-----------|---------|-----------|----------|----------|----------|
| US | May.02 | Feb.02 | Jun.02 | Feb.02 | Jan.01 |
| EU(UK) | Sep.02 | Dec.02 | | 5/22/02 | 10/3/02 |
| Australia | 8/12/02 | 4/22/02 | 10/19/01 | 4/5/02 | 10/10/01 |
| Japan | Jul.02 | Sep.02 | | | Nov.02 |
| Canada | 3/17/03 | 2002 | | 6/16/00 | 2001 |

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Hyperglycaemia

Global labels:

Zyprexa: SPC Warning EU (07/99), US (ADR), Japan (04/02, CI), Australia (08/02), Korea (03/03)

Canada (03/03)

Seroquel: SPC Warning Sweden, Denmark (02/03), US (ADR), Japan (11/02, CI), NZ (06/02), Ireland (04/03)

Risperdal: SPC Warning UK (12/02), US (ADR), Japan (ADR, 09/02), Australia (08/02), Ireland (06/03)

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Zyprexa label Overview for DM

| | US | EU | Australia | Japan | Canada |
|---------------------------|----|----|-----------|-------|--------|
| Black Box | | | | | |
| Contraindication | | | | √ | |
| Warning | | √* | | √ | |
| Precaution | | √* | √ | √ | √ |
| Adverse Reaction | √ | √ | √ | √ | √ |
| Post Introduction Reports | √ | √ | √ | | |

* In EU's label, warnings and precautions are in one paragraph

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Psychotropic Label Overview for DM

| | Zyprexa | Risperdal | Geodon | Clozaril | Seroquel |
|------------------------------|-------------------|--|--------|---------------|--------------------|
| Black Box | | | | | |
| Contraindication | Jp | | | | Jp |
| Warning | Jp, EU Kor | | | | Jp, Sw, Den, Ir |
| Precaution | EU, Au, Jp | Jp* | | US, Au, Ca | Jp |
| Adverse Reaction | US, EU, Au, Jp | US, Au, UK, Jp*, Netherland, Sweden | US | EU, Au, Ca | US, Jp, NZ |
| Post Introduction Reports | US, EU | US | | US | |

*Hyperglycemia is listed in other adverse reactions under Precautions based on English translation of excerpts from "Notice of Revision of Precautions" issued by Janssen in Sep.2002

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US Psychotropic Label for DM

| Product (Revision date) | Zyprexa (May. 02) | Risperdal (Feb. 02) | Geodon (Jun.02) | Clozaril (Feb.02) | Seroquel (Jan 01) |
|------------------------------|----------------------|------------------------|--------------------|----------------------|----------------------|
| Black Box | | | | | |
| Contraindication | | | | | |
| Warning | | | | | |
| Precaution | | | | √ | |
| Adverse Reaction | √ | √ | √ | | √ |
| Post Introduction Reports | √ | √ | | √ | |

Source: Analysis from latest PI of Apr 03

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EU Psychotropic Label for DM

| Product (Revision Date) | Zyprexa (Sep.02) | Risperdal (Dec.02) | Geodon* | Clozaril (5/22/02) | Seroquel (10/3/02) |
|------------------------------|---------------------|-----------------------|---------|-----------------------|-----------------------|
| Black Box | | | | | |
| Contraindication | | | | | |
| Warning | | | | | |
| Precaution | √ | | | | |
| Adverse Reaction | √ | √ | | √ | |
| Post Introduction Reports | √ | | | | |

*Geodon is not on the market

Risperdal, Geodon, Clozaril and Seroquel are used UK PI as reference
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Australia Psychotropic Label for DM

| Product (Revision Date) | Zyprexa (8/12/02) | Risperdal (4/22/02) | Geodon (10/19/01) | Clozaril (4/5/02) | Seroquel (10/10/01) |
|------------------------------|----------------------|------------------------|----------------------|----------------------|------------------------|
| Black Box | | | | | |
| Contraindication | | | | | |
| Warning | | | | | |
| Precaution | √ | | | √ | |
| Adverse Reaction | √ | √ | | √ | |
| Post Introduction Reports | | | | | |

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Japan Psychotropic Label for DM

| Product (Revision Date) | Zyprexa (Jul 02) | Risperdal (Sep 02) | Geodon** | Clozaril** | Seroquel (Nov 02) |
|------------------------------|---------------------|-----------------------|----------|------------|----------------------|
| Black Box | | | | | |
| Contraindication | √ | | | | √ |
| Warning | √ | | | | √ |
| Precaution | √ | √* | | | √ |
| Adverse Reaction | √ | √* | | | √ |
| Post Introduction Reports | | | | | |

*Hyperglycemia is listed in other adverse reactions under Precautions based on English translation of excerpts from “Notice of Revision of Precautions” issued by Janssen in Sep.2002

**Geodon and Clozaril are not on the market

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Canada Psychotropic Label for DM

| Product (Revision Date) | Zyprexa (3/17/03) | Risperdal 2002 | Geodon* | Clozaril (6/16/00) | Seroquel 2001 |
|------------------------------|----------------------|-------------------|---------|-----------------------|------------------|
| Black Box | | | | | |
| Contraindication | | | | | |
| Warning | | | | | |
| Precaution | √ | | | √ | |
| Adverse Reaction | √ | | | √ | |
| Post Introduction Reports | | | | | |

* Geodon is not on the market

Source: Analysis from latest PI of Apr 03

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Zyprexa DM Label Comparison for Brand Council Affiliates

| | US | European Union | Australia | Japan | Canada |
|------------------|----|----------------|-----------|--|--------|
| Black Box | NA | NA | NA | NA | NA |
| Contraindication | NA | NA | NA | Patients with diabetes mellitus and those who have a history of diabetes mellitus | NA |
| Warnings | NA | NA | NA | <p>1.From marked increase in blood glucose, serious adverse reaction such as diabetic ketoacidosis, diabetic coma etc.may appear leading potentially to death.Observe sufficiently with such as measurement of blood glucose during the olanzapine administration</p> <p>2.Upon administration, explain sufficiently in advance to the patient and family members possible occurrence of above adverse reactions. Provide guidance to them to pay attention to such abnormalities as thirst, polydipsia, polyurea, frequent urination, etc., and to see a physician suspending administration immediately if such symptoms appear.</p> | |

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Zyprexa DM Label Comparison for Brand Council Affiliates

| | US | European Union | Australia | Japan | Canada |
|-------------|----|---|---|--|--|
| Precautions | NA | <p>Special warning and special precaution for use:</p> <p>Hyperglycaemia or exacerbation of pre-existing diabetes occasionally associated with ketoacidosis or coma has been reported very rarely, including some fatal case. In some cases, a prior increase in body weight has been reported which may be a predisposing factor. Appropriate clinical monitoring is advisable in diabetic patients and in patients with risk factors for the development of diabetes mellitus</p> | <p>There is an increased prevalence of diabetes in patients with schizophrenia. As with some other antipsychotics, exacerbation of pre-existing diabetes has been reported very rarely. Hyperglycaemia, diabetic coma and diabetic ketoacidosis have been reported in very rare cases, sometimes in patients with no reported history of hyperglycaemia (see ADVERSE REACTIONS). Appropriate clinical monitoring is advisable in diabetic patients.</p> | <p>Careful Administration (This product should be administered with care in the following patients.)</p> <p>Patients with risk factors for diabetes mellitus such as family history of diabetes mellitus, hyperglycemia obesity, etc.</p> <p>Important Precaution</p> <p>1) By administration of this drug, marked increase in blood glucose may appear leading to fatal clinical course such as diabetic ketoacidosis, diabetic coma, etc. Observe sufficiently with such as measurement of blood glucose, (appearance of thirst, polydipsia, polyurea, and frequent urination during the olanzapine administration. In particular, patients with risk factors for diabetes mellitus such as hyperglycemia, obesity, etc., blood glucose may increase, leading to acute worsening of metabolic state.</p> <p>2) Upon administration, explain sufficiently in advance to the patient and family members possible occurrence of above adverse reactions. Provide guidance to them to pay attention to such abnormalities as thirst, polydipsia, polyurea, frequent urination, etc., and to see a physician suspending administration immediately if such symptoms appear.</p> | <p>As with some other antipsychotics, exacerbation of pre-existing diabetes, hyperglycaemia, diabetic ketoacidosis, and diabetic coma including some fatal cases have been reported very rarely during the use of ZYPREXA, sometimes in patients with no reported history of hyperglycaemia (see ADVERSE REACTIONS; Post-Market Experience). In some cases, a prior increase in body weight has been reported which may be a predisposing factor. Appropriate clinical monitoring is advisable in diabetic patients and in patients with risk factors for the development of diabetes mellitus.</p> <p><i>Use in Patients with Diabetes and Risk Factors for Development of Diabetes:</i></p> <p>As with some other antipsychotics, exacerbation of pre-existing diabetes, hyperglycaemia, diabetic ketoacidosis, and diabetic coma including some fatal cases have been reported very rarely during the use of ZYPREXA, sometimes in patients with no reported history of hyperglycaemia (see ADVERSE REACTIONS; Post-Market Experience). In some cases, a prior increase in body weight has been reported which may be a pre-disposing factor. Appropriate clinical monitoring is advisable in diabetic patients and in patients with risk factors for the development of diabetes mellitus.</p> |

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Zyprexa DM Label Comparison for Brand Council Affiliates

| | US | European Union | Australia | Japan | Canada |
|---------------------------|---|--|--|---|--------|
| Adverse Reactions | Endocrine System-- Infrequent: diabetes mellitus; Rare: diabetic acidosis. Metabolic and Nutritional Disorders-- Infrequent: acidosis, hyperglycemia, hypoglycemia; Rare: ketosis. | Undesirable effects: ¹ In clinical trials with olanzapine in over 5000 patients with baseline non-fasting glucose levels ≤ 7.8 mmol/l, the incidence of non-fasting plasma glucose levels ≥ 11 mmol/l (suggestive of diabetes) was 1.0%, compared to 0.9% with placebo. The incidence of non-fasting plasma glucose levels ≥ 8.9 mmol/l but < 11 mmol/l (suggestive of hyperglycaemia) was 2.0%, compared to 1.6% with placebo. Hyperglycaemia is also reported as a Very Rare ($<0.01\%$) spontaneous event. Metabolism and nutrition disorders <i>Very rare ($<0.01\%$):</i> Hyperglycaemia or exacerbation of pre-existing diabetes occasionally associated with ketoacidosis or coma has been spontaneously reported very rarely, including some fatal cases Common(1-10%): Elevated glucose levels. | Clinical chemistry – Common ($\geq 1\%$ and $< 10\%$): In clinical trials with olanzapine in over 5000 patients with baseline non-fasting glucose levels ≤ 7.8 mmol/L, the incidence of non-fasting plasma glucose levels ≥ 11 mmol/L (suggestive of diabetes) was 1.0%, compared to 0.9% with placebo. The incidence of non-fasting plasma glucose levels ≥ 8.9 mmol/L but < 11 mmol/L (suggestive of hyperglycaemia) was 2.0%, compared to 1.6% with placebo <u>Adverse events identified from spontaneous post marketing surveillance</u> Metabolic- Very rare ($<0.01\%$): Hyperglycaemia;diabetic coma;diabetic | Clinically significant adverse reactions Hyperglycemia, Diabetic ketoacidosis, Diabetic coma: Hyperglycemia may develop leading to fatal clinical course, such as diabetic ketoacidosis and diabetic coma leading to death. Thus, make a close observation, with such as blood glucose measurement,(appearance of) thirst,polydipsia,polyurea and frequent urination.If any abnormalities are noted,discontinue administration and take an appropriate measure(s)such as administration of insulin Other adverse reactions Japanese clinical studies and postmarketing reports Metabolic : $<1\%$: Diabetes Foreign clinical studies and postmarketing spontaneous reports Metabolic: $<10\%$ and $\geq 1\%$: Hyperglycemia ^{notes1, 6)} Unknown: Coma diabetic, Diabetic ketoacidosis 1) As assessed by measured values within the clinical trial database 6) Casual blood glucose: Not less than 160 mg/dL | NA |
| Post introduction Reports | Diabetic coma | Very rare ($<0.01\%$): Hyperglycaemia or exacerbation of pre-existing diabetes occasionally associated with ketoacidosis or coma has been spontaneously reported very rarely, including some fatal cases. | NA | NA | NA |

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US Psychotropic Label Wording for DM

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| | Zyprexa | Risperdal | Geodon | Clozaril | Seroquel |
|---------------------------|---|---|--|---|--|
| Black Box | NA | NA | NA | NA | NA |
| Contraindication | NA | NA | NA | NA | NA |
| Warnings | NA | NA | NA | NA | NA |
| Precautions | NA | NA | NA | Hyperglycemia: Severe hyperglycemia, sometimes leading to ketoacidosis, has been reported during CLOZARIL treatment in patients with no prior history of hyperglycemia. While a causal relationship to CLOZARIL use has not been definitively established, glucose levels normalized in most patients after discontinuation of CLOZARIL, and a rechallenge in one patient produced a recurrence of hyperglycemia. The effect of CLOZARIL on glucose metabolism in patients with diabetes mellitus has not been studied. The possibility of impaired glucose tolerance should be considered in patients receiving CLOZARIL who develop symptoms of hyperglycemia, such as polyuria, polyphagia, and weakness. In patients with significant treatment-emergent hyperglycemia, the discontinuation of CLOZARIL should be considered. | |
| Adverse Reactions | Endocrine System-- Infrequent: diabetes mellitus; Rare: diabetic acidosis. Metabolic and Nutritional Disorders-- Infrequent: acidosis, hyperglycemia, hypoglycemia; Rare: ketosis. | Metabolic and Nutritional Disorders: Infrequent: diabetes mellitus. Rare: hypoglycemia | Metabolic and Nutritional Disorders: Infrequent: hyperglycemia; Rare: hypoglycemia, glucose tolerance decreased, hypoglycemic reaction, ketosis | NA | Metabolic and Nutritional System: Infrequent: hyperglycemia, hypoglycemia. Endocrine System: Infrequent: diabetes mellitus. |
| Post introduction Reports | Diabetic coma | Hyperglycemia, Diabetes mellitus aggravated, including diabetic ketoacidosis | NA | Miscellaneous: hyperglycemia | NA |

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European Union Psychotropic Label Wording for DM

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| | Zyprexa | Risperdal | Geodon* | Clozaril | Seroquel |
|---------------------------|--|---|---------|---|----------|
| Black Box | NA | NA | | NA | NA |
| Contraindication | NA | NA | | NA | NA |
| Warnings | NA | NA | | NA | NA |
| Precautions | Special warning and special precaution for use: Hyperglycaemia or exacerbation of pre-existing diabetes occasionally associated with ketoacidosis or coma has been reported very rarely, including some fatal case. In some cases, a prior increase in body weight has been reported which may be a predisposing factor. Appropriate clinical monitoring is advisable in diabetic patients and in patients with risk factors for the development of diabetes mellitus | NA | | NA | NA |
| Adverse Reactions | Undesirable effects: ¹ In clinical trials with olanzapine in over 5000 patients with baseline non-fasting glucose levels ≤ 7.8 mmol/l, the incidence of non-fasting plasma glucose levels ≥ 11 mmol/l (suggestive of diabetes) was 1.0%, compared to 0.9% with placebo. The incidence of non-fasting plasma glucose levels ≥ 8.9 mmol/l but < 11 mmol/l (suggestive of hyperglycaemia) was 2.0%, compared to 1.6% with placebo. Hyperglycaemia is also reported as a Very Rare ($<0.01\%$) spontaneous event. Metabolism and nutrition disorders <i>Very rare (<0.01%):</i> Hyperglycaemia or exacerbation of pre-existing diabetes occasionally associated with ketoacidosis or coma has been spontaneously reported very rarely, including some fatal cases <i>Common(1-10%):</i> Elevated glucose levels. | Hyperglycaemia and exacerbation of pre-existing diabetes have been reported in very rare cases during risperidone treatment | | Abnormalities of glucose homeostasis occur uncommonly in approximately 0.35% of CLOZARIL (clozapine) patients in the UK cohort monitored by the CLOZARIL Patient Monitoring Service. Severe hyperglycaemia, sometimes leading to ketoacidosis, has been reported during CLOZARIL (clozapine) treatment in patients with no prior history of hyperglycaemia. Blood glucose levels normalised in most patients after discontinuation of CLOZARIL (clozapine), and a rechallenge in a few cases produced a recurrence of hyperglycaemia. The possibility of impaired glucose tolerance should be considered in patients receiving CLOZARIL (clozapine) particularly if symptoms of polydipsia, polyuria, and weakness develop. With prolonged treatment considerable weight gain has been observed in some patients and further investigation is periodically needed to ensure hyperglycaemia is not missed. In patients with significant treatment-emergent hyperglycaemia, the discontinuation of CLOZARIL (clozapine) should be considered when active medical management of the hyperglycaemia has failed. | |
| Post introduction Reports | Very rare ($<0.01\%$): Hyperglycaemia or exacerbation of pre-existing diabetes occasionally associated with ketoacidosis or coma has been spontaneously reported very rarely, including some fatal cases. | NA | | NA | NA |

*Geodon is not on the market

Risperdal, Geodon, Clozaril and Seroquel are used UK PI as reference

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Australia Psychotropic Label Wording for DM

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| | Zyprexa | Risperdal | Geodon | Clozaril | Seroquel |
|---------------------------|--|--|--------|--|----------|
| Black Box | NA | NA | NA | NA | NA |
| Contraindication | NA | NA | NA | NA | NA |
| Warnings | NA | NA | NA | NA | NA |
| Precautions | There is an increased prevalence of diabetes in patients with schizophrenia. As with some other antipsychotics, exacerbation of pre-existing diabetes has been reported very rarely. Hyperglycaemia, diabetic coma and diabetic ketoacidosis have been reported in very rare cases, sometimes in patients with no reported history of hyperglycaemia (see ADVERSE REACTIONS). Appropriate clinical monitoring is advisable in diabetic patients. | NA | NA | On rare occasions, severe hyperglycaemia, sometimes leading to ketoacidosis/hypersomolar coma, has been reported during Clozaril treatment in patients with no prior history of hyperglycaemia. While a causal relationship to Clozaril use has not been definitely established, glucose levels returned to normal in most patients after discontinuation of Clozaril, and rechallenge produced a recurrence of hyperglycaemia in a few cases. The effect of Clozaril on glucose metabolism in patients with diabetes mellitus has not been studied. The possibility of impaired glucose tolerance should be considered in patients receiving Clozaril who develop symptoms of hyperglycaemia, such as polydipsia, polyuria, polyphagia or weakness. In patients with significant treatment-emergent hyperglycaemia, discontinuation of Clozaril should be considered. | NA |
| Adverse Reactions | Clinical chemistry – <u>Common (≥ 1% and < 10%):</u> In clinical trials with olanzapine in over 5000 patients with baseline non-fasting glucose levels ≤7.8 mmol/L, the incidence of non-fasting plasma glucose levels ≥11mmol/L (suggestive of diabetes) was 1.0%, compared to 0.9% with placebo. The incidence of non-fasting plasma glucose levels ≥8.9mmol/L but <11mmol/L (suggestive of hyperglycaemia) was 2.0%, compared to 1.6% with placebo <u>Adverse events identified from spontaneous post marketing surveillance</u> Metabolic- Very rare (<0.01%): Hyperglycaemia;diabetic coma;diabetic ketoacidosis;exacerbation of pre-existing diabetes. | Hyperglycaemia and exacerbations of pre-existing diabetes have been reported in very rare cases during risperidone treatment | NA | Severe hyperglycaemia, sometimes leading to ketoacidosis/hyperosmolar coma, has been reported rarely during Clozaril treatment in patients with no prior history of hyperglycaemia | |
| Post introduction Reports | | NA | NA | NA | NA |

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Japan Psychotropic Label Wording for DM

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| | Zyprexa | Risperda 1** | Geodon * | Clozari 1* | Seroquel ** |
|------------------|---|--|-------------|---------------|---|
| Black Box | NA | NA | | | NA |
| Contraindication | Patients with diabetes mellitus and those who have a history of diabetes mellitus | NA | | | Diabetes mellitus history of diabetes mellitus have been added on the section of contraindication |
| Warnings | 1.From marked increase in blood glucose, serious adverse reaction such as diabetic ketoacidosis, diabetic coma etc.may appear leading potentially to death.Observe sufficiently with such as measurement of blood glucose during the olanzapine administration 2.Upon administration, explain sufficiently in advance to the patient and family members possible occurrence of above adverse reactions. Provide guidance to them to pay attention to such abnormalities as thirst, polydipsia, polyurea, frequent urination, etc., and to see a physician suspending administration immediately if such symptoms appear. | NA | | | Diabetes mellitus history of diabetes mellitus have been added on the section of warning |
| Precautions | Careful Administration (This product should be administered with care in the following patients.) Patients with risk factors for diabetes mellitus such as family history of diabetes mellitus, hyperglycemia obesity,etc. Important Precaution 1)By administration of this drug, marked increase in blood glucose may appear leading to fatal clinical course such as diabetic ketoacidosis, diabetic coma, etc. Observe sufficiently with such as measurement of blood glucose,(appearance of thirst, polydipsia, polyurea, and frequent urination during the olanzapine administration. In particular, patients with risk factors for diabetes mellitus such as hyperglycemia,obesity,etc.,blood glucose may increase, leading to acute worsening of metabolic state. 2) Upon administration, explain sufficiently in advance to the patient and family members possible occurrence of above adverse reactions. Provide guidance to them to pay attention to such abnormalities as thirst, polydipsia, polyurea, frequent urination, etc., and to see a physician suspending administration immediately if such symptoms appear. | “Hyperglycemia” has been added on the section of “Other adverse reaction” under Precautions by Janssen | | | Diabetes mellitus and Hyperglycemia has been added on the section of Precaution |

*Geodon and Clozaril are not on the market

**the language was translated by ELJKK from Japanese to English that were released by Janssen and AZ for the label changes for their respective products.

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| | Zyprexa | Risperda l** | Geo don * | Clo zari l* | Seroquel ** |
|---------------------------|---|-----------------|-----------------|-------------------|---|
| Adverse Reactions | <p>Clinically significant adverse reactions Hyperglycemia, Diabetic ketoacidosis, Diabetic coma: Hyperglycemia may develop leading to fatal clinical course, such as diabetic ketoacidosis and diabetic coma leading to death. Thus, make a close observation, with such as blood glucose measurement,(appearance of) thirst,polydipsia,polyurea and frequent urination.If any abnormalities are noted,discontinue administration and take an appropriate measure(s)such as administration of insulin</p> <p>Other adverse reactions</p> <p>Japanese clinical studies and postmarketing reports Metabolic : <1%: Diabetes</p> <p>Foreign clinical studies and postmarketing spontaneous reports Metabolic: <10% and ≥1%: Hyperglycemia^{notes1, 6)} Unknown: Coma diabetic, Diabetic ketoacidosis 1) As assessed by measured values within the clinical trial database 6) Casual blood glucose: Not less than 160 mg/dL</p> | NA | | | Diabetes and hyperglycemia as been added on the section of “Other adverse reactions” by AstraZeneca |
| Post introduction Reports | NA | NA | | | NA |

*Geodon and Clozaril are not on the market

**the language was translated by ELJJKK from Japanese to English that were released by Janssen and AZ for the label changes for their respective products.

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Canada Psychotropic Label Wording for DM

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| | Zyprexa | Risperdal | Geodon * | Clozaril | Seroquel |
|---------------------------|--|-----------|----------|--|----------|
| Black Box | NA | NA | | NA | NA |
| Contraindication | NA | NA | | NA | NA |
| Warnings | NA | NA | | NA | NA |
| Precautions | <p>As with some other antipsychotics, exacerbation of pre-existing diabetes, hyperglycaemia, diabetic ketoacidosis, and diabetic coma including some fatal cases have been reported very rarely during the use of ZYPREXA, sometimes in patients with no reported history of hyperglycaemia (see ADVERSE REACTIONS; Post-Market Experience). In some cases, a prior increase in body weight has been reported which may be a predisposing factor. Appropriate clinical monitoring is advisable in diabetic patients and in patients with risk factors for the development of diabetes mellitus.</p> <p><i>Use in Patients with Diabetes and Risk Factors for Development of Diabetes:</i></p> <p>As with some other antipsychotics, exacerbation of pre-existing diabetes, hyperglycaemia, diabetic ketoacidosis, and diabetic coma including some fatal cases have been reported very rarely during the use of ZYPREXA, sometimes in patients with no reported history of hyperglycaemia (see ADVERSE REACTIONS; Post-Market Experience). In some cases, a prior increase in body weight has been reported which may be a pre-disposing factor. Appropriate clinical monitoring is advisable in diabetic patients and in patients with risk factors for the development of diabetes mellitus.</p> | NA | | <p>Hyperglycemia</p> <p>On rare occasions, severe hyperglycemia, sometimes leading to ketoacidosis, has been reported during Clozaril treatment in patients with no prior history of hyperglycemia. While a causal relationship to Clozaril use has not been definitely established, glucose levels returned to normal in most patients after discontinuation of Clozaril, and rechallenge produced a recurrence of hyperglycemia in a few cases. The effect of Clozaril on glucose metabolism in patients with diabetes mellitus has not been studied. The possibility of impaired glucose tolerance should be considered in patients receiving Clozaril who develop symptoms of hyperglycemia, such as polydipsia, polyuria, polyphagia or weakness. In patients with significant treatment-emergent hyperglycemia, discontinuation of Clozaril should be considered</p> | |
| Adverse Reactions | NA | NA | | On rare occasions, severe hyperglycemia, sometimes leading to ketoacidosis, has been reported during Clozaril treatment in patients with no prior history of hyperglycemia | NA |
| Post Introduction Reports | NA * introduction not on the market | NA | | NA | NA |

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