VI.2 Elements for a Public Summary

VI.2.1 Overview of Disease Epidemiology

Schizophrenia is a severe form of mental illness affecting about 7 per thousand of the adult population, mostly in the age group 15-35 years. Up to 10,000 new cases are reported each year. Schizophrenia affects about 24 million people worldwide. The disease is more prevalent among males than females.

Schizophrenia is a treatable disorder, with treatment being more effective in its initial stages. More than 50% of patients with schizophrenia are not receiving appropriate care. 90% of people with untreated schizophrenia are in developing countries. Care of patients with schizophrenia can be provided at community level, with active family and community involvement.

VI.2.2 Summary of treatment benefits

Schizoprenia is treated with antipsychotic drugs. There are two main groups of antipsychotics, the first called “typical” or “first generation” and the second group called “atypical” or second generation. Amisulpride belongs to the second group of antipsychotics.

Both groups affect the action of a number of chemicals in the brain called neurotransmitters – chemicals which brain cells need to communicate with each other. Dopamine is the main neurotransmitter affected by these medications. It is involved in how we feel: that something is significant, important or interesting; satisfaction; motivation.

A recent multiple treatment meta-analysis has been performed on the efficacy and tolerability of 15 different antipsychotic drugs including amisulpride. The findings showed that all drugs were effective but differed in the numbers and types of side-effects.

As individuals react differently to the various antipsychotics, particularly regarding side-effects, it can often take some time, negotiation and ‘trial and error’ to find the best antipsychotic for a particular person.

VI.2.3 Unknown relating to treatment benefits

Limited information is available on use of amisulpride in the paediatric population, in patients with severe renal impairment, in patients with hepatic impairment, and in pregnant and lactating women.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	**What is known**	**Preventability**
Neuroleptic Malignant Syndrome	Neuroleptic malignant syndrome is a rare but potentially fatal side effect that can occur with antipsychotic agents, including amisulpride.	Patients should tell their doctor immediately if: • they have high fever, muscle stiffness, impaired awareness and strong sweating. These can be fatal and require immediate medical attention
Hyperglycaemia and diabetes mellitus	Hyperglycaemia is an uncommon side effect that can occur with antipsychotic agents, including amisulpride. in patients with an established diagnosis of diabetes mellitus.	Patients should be advised to notify their doctor if: they are diabetic or have been told they are at risk of having diabetes
Hypotension and sedation in elderly	In elderly patients, amisulpride, like other antipsychotic agents, should be used with particular caution because of a possible risk of hypotension and sedation. Reduction in dosage may also be required because of renal insufficiency.	Patients should be advised to notify their doctor if: • they have heart disease or family history of heart problems
Prolongation of the QT interval	QT prolongation is a common side effect that can occur when amisulpride is prescribed in patients with known cardiovascular disease or family history of irregular heartbeats (long QT syndrome)	Patients should be advised to notify their doctor if someone in their family has a rare inherited heart disease with slow heart rate and irregular heartbeats (long QT syndrome).
Leukopenia, neutropenia, agranulocytosis	Leukopenia, neutropenia and agranulocytosis (low number of blood cells) are side effects that can occur with antipsychotic agents, including amisulpride.	Patients should be advised to notify their doctor if: they experience general malaise, they have a tend to inflammation, especially

		tonsillitis and fever (infections), because of a low number of white blood cells (agranulocytosis). Patients should be advised to stop taking Product Name and see a doctor or go to a hospital straight away if: • they get more infections than usual. This could be because of a blood disorder (agranulocytosis) or a decrease in the number of white blood cells (neutropenia)
Withdrawal symptoms	Acute withdrawal symptoms including nausea, vomiting and insomnia have been described after abrupt cessation of high doses of antipsychotic drugs, including amisulpride.	It is recommended that patients keep taking Product Name until their doctor tells them to stop. If they suddenly stop the treatment, after high doses of amisulpride, nausea, vomiting and insomnia may occur. Reappearance of the symptoms that they are treated for and involuntary movement disorders (such as akathisia, dystonia and dyskinesia) may also occur.
Weight gain	Weight gain is a common side effect that can occur with antipsychotic agents, including amisulpride.	Among the side effects of amisulpride, weight gain is a common one.
Torsades de pointes	Ventricular arrhythmias such as torsade de pointes, ventricular tachycardia, which may result in ventricular fibrillation or cardiac arrest, sudden death are rare side effects that can occur with amisulpride.	Patients should be advised to notify their doctor if: • they have heart disease or family history of heart problems
Drug-drug interactions with levodopa, dopamine	QT prolongation is a common side effect that can occur when amisulpride is prescribed in patients who are also taking levodopa, a medicine to treat	In particular, patients should not take this medicine if

agonists, CNS depressants, antihypertensive drugs and other hypotensive medications and medicine known to prolong the QT interval	Parkinson's disease; • medicines called dopamine agonists (e.g. bromocriptine, ropinirole); • medicines for heart rhythm disturbances (for example amiodarone, sotalol, quinidine, disopyramide);	they are on a treatment with: • Levodopa, a medicine to treat Parkinson's disease. •Medicines called dopamine agonists (e.g. bromocriptine, ropinirole) • Medicines for heart rhythm disturbances (e.g. amiodarone, sotalol, quinidine, disopyramide). •Other medicines such as bepridil, cisapride, sultopride, thioridazine, methadone, erythromycin IV, vincamin iv, halofantrine, pentamidine, sparfloxacin
Extrapyramidal symptoms	Extrapyramidal symptoms (tremor, rigidity, hypokinesia, hypersalivation, akathisia, dyskinesia) are very common side effects. These symptoms are generally mild at optimal dosages and partially reversible without discontinuation of amisulpride upon administration of antiparkinsonian medication.	It is recommended that patients keep taking Product Name until their doctor tells them to stop. If they suddenly stop the treatment, after high doses of amisulpride, nausea, vomiting and insomnia may occur. Reappearance of the symptoms that they are treated for and involuntary movement disorders (such as akathisia, dystonia and dyskinesia) may also occur.
Acute dystonia	Acute dystonia (spasm torticollis, oculogyric crisis, trismus) is a common side effect of amisulpride and reversible without discontinuation of amisulpride upon treatment with an antiparkinsonian agent.	It is recommended that patients keep taking Product Name until their doctor tells them to stop. If they suddenly stop the treatment, after high doses of amisulpride, nausea,

		vomiting and insomnia may occur. Reappearance of the symptoms that they are treated for and involuntary movement disorders (such as akathisia, dystonia and dyskinesia) may also occur.
Tardive dyskinesia	Tardive dyskinesia (characterized by rhythmic, involuntary movements primarily of the tongue and/or face) is an uncommon side effect that have been reported, usually after long term administration or withdrawal of amisulpride.	It is recommended that patients keep taking Product Name until their doctor tells them to stop. If they suddenly stop the treatment, after high doses of amisulpride, nausea, vomiting and insomnia may occur. Reappearance of the symptoms that they are treated for and involuntary movement disorders (such as akathisia, dystonia and dyskinesia) may also occur.
Worsening of Parkinson's disease	Worsening of Parkinson's disease may occur with amisulpride, as with other antipsychotic agents, and caution should be exercised when prescribing amisupride to patients with Parkinson's disease.	Patients should be advised to notify their doctor if: • they have Parkinson's disease
Cerebrovascular events	In elderly patients with dementia and treated with certain atypical antipsychotic agents, an increase of the risk of cerebrovascular events has been observed.	Certain patient groups (for example, elderly and patients with dementia) have greater risk of side effects, including stroke.
Venous thromboembolism	Venous thromboembolism is a side effect which may occur with antipsychotic agents, including amisulpride, with frequency not known.	Patients should be advised to notify their doctor if someone in their family has a rare inherited heart disease with slow heart rate and irregular heartbeats (long QT syndrome). Talk to their doctor especially if: • they or someone else in their family has a history of blood clots (thrombosis), as medicines like these have been associated with

		formation of blood clots (thrombi).
Withdrawal symptoms in neonates	Withdrawal symptoms in neonates are side effects that can occur when using antipsychotic agents, including amisulpride, with the frequency not known	The following symptoms may occur in newborn babies, of mothers that have used amisulpride in the last trimester (last three months of their pregnancy): • shaking, muscle stiffness • weakness, sleepiness, agitation, breathing problems, • difficulty in feeding. If the baby develops any of these symptoms the mother may need to contact her doctor.
Death in elderly patients with dementia	Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death.	Certain patient groups (e.g. elderly and patients with dementia) has greater risk of side effects, including stroke.
Use in paediatric population	The use of amisulpride from puberty to the age of 18 years is not recommended because of limited data.	Product Name should not be given to children before puberty.
Use in patients with severe renal impairment	Particular care is recommended in patients with severe renal impairment (CRCL < 10 ml/min).	People with kidney problems The doctor may reduce the dose. The patient should follow the doctor's instructions.
Use in pregnancy and lactation	The safety of amisulpride during human pregnancy has not been established. Use of the drug is not recommended during pregnancy unless the benefits justify the potential risks. Very limited clinical data on exposed pregnancies are available. It is not known whether Product Name is excreted	If the patient is pregnant or breast-feeding, think she might be pregnant or are planning to have a baby, she should ask her doctor or pharmacist for advice before taking this medicine.

	in breast milk, breast-feeding is therefore contra-indicated.	The following symptoms may occur in newborn babies, of mothers that have used Product Name in the last trimester (last three months of their pregnancy): • shaking, muscle stiffness • weakness, sleepiness, agitation, breathing problems, • difficulty in feeding. If your baby develops any of these symptoms you may need to contact your doctor. Product Name should not be taken during breast-feeding.
Use in hepatic impairment	Since the drug is weakly metabolised a dosage reduction should not be necessary.	Hepatic insufficiency A dosage reduction is not necessary.

Summary of risk minimisation activities by safety concern

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

This medicine has no additional risk minimisation measures.

Planned post-authorisation development plan

None.

Summary of changes to the risk management plan over time

Not applicable.