AUSTRALIAN PRODUCT INFORMATION – PFIZER (AUSTRALIA) GLUCOSE INTRAVENOUS INFUSION BP 5% (GLUCOSE (AS MONOHYDRATE))

1. NAME OF THE MEDICINE

Glucose monohydrate

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each mL of solution contains 54.99 mg glucose monohydrate (equivalent to 50 mg glucose). When necessary, pH is adjusted with sodium hydroxide and/or hydrochloric acid. pH is 3.5 to 6.5 and osmolality 250 to 350 mOsm/kg.

For the full list of excipients, see Section 6.1 List of excipients.

3. PHARMACEUTICAL FORM

Injection, intravenous infusion.

Sterile isotonic preservative-free solutions containing glucose monohydrate.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

- For fluid and carbohydrate depletion wherever a non-electrolyte fluid is required
- In the treatment of hypoglycaemia
- In the treatment of acute diarrhoeal disease
- As a vehicle for the administration of other medications

4.2 Dose and method of administration

Dosage

Dosage will be dependent upon individual patient circumstances, such as age, weight and clinical condition and is determined by the attending physician.

Method of administration

The infusion rate should not exceed 0.5 g/kg/hour to avoid potential glycosuria.

Glucose Intravenous Infusion BP 5% may be administered via a peripheral vein, preferable large arm vein and the site of infusion should be changed daily if more than one infusion is required.

Do not use if any visible particles are observed.

4.3 Contraindications

- Patients with clinically significant hyperglycaemia.
- Glucose-Galactose Malabsorption Syndrome.
- Diabetic coma where blood sugar levels are excessively high.
- Avoid use in ischaemic stroke, as under this condition, the induced lactic acidosis aggravates the recovery of the damaged brain tissue.
- Patients who have had head trauma within 24 hours, with blood glucose concentrations being closely monitored during intracranial hypertension.
- Intracranial or intraspinal haemorrhage.
- Patients with delirium tremens who are severely dehydrated.
- Patients who are anuric.
- Patients with known hypersensitivity to the product.
- Patients who are known to have an allergy reaction to corn (maize) or corn products.

4.4 Special warnings and precautions for use

General

- Glucose injections, even if iso-osmotic, should not be mixed with whole blood as haemolysis and agglomeration may occur.
- Additives may be incompatible with glucose. Do not administer such preparations unless the solution is clear. Do not store solutions containing additives unless compatibility has been proven. While some incompatibilities are readily observed, one must be aware that subtle physical, chemical and pharmacological incompatibilities can occur. The medical literature, the package insert and other available sources of information should be reviewed for a thorough understanding of possible incompatibility problems. In particular, the product information document of any added medication should be checked for any incompatibility with the glucose infusion.
- Hyperglycaemia and glycosuria may occur in patients with metabolic insufficiency or as a result of an over rapid rate infusion.
- Prolonged parenteral administration of glucose may affect insulin production. To avoid this it may be necessary to add insulin to the infusion.

- When used as a vehicle of drug delivery, the product information document of the drug(s) for infusion should be examined to ensure compatibility with the solution.

- Administration of a substantially hypertonic solution may lead to a wide variety of complications. These include crenation (shrinkage) of red blood cells and general cellular dehydration. Thus, unless appropriately diluted, the infusion of hypertonic glucose injection solution into a peripheral vein may result in vein irritation, vein damage, and thrombosis. Strongly hypertonic nutrient solutions should only be administered through an indwelling intravenous catheter with the tip located in a large central vein such as the superior vena cava.

- Similarly, administration of hypertonic glucose injection and amino acid solutions via central venous catheter may be associated with complications that can be prevented or minimised by careful attention to all aspects of the procedure.

- Caution should be exercised in the administration of the glucose intravenous injection containing sodium ions to patients receiving corticosteroids or corticotropin as it may lead to hypernatraemia.

Hypersensitivity reactions

Hypersensitivity/infusion reactions, including anaphylactic/anaphylactoid reactions, have been reported with glucose intravenous infusions. The infusion must be stopped immediately if any signs or symptoms of a suspected hypersensitivity reaction develop. Appropriate therapeutic countermeasures must be instituted as clinically indicated.

Dilution and other effects on serum electrolytes

The administration of Glucose Intravenous Infusion BP 5% can cause fluid and/or solute overloading resulting in dilution of the serum electrolyte concentrations, over-hydration, congested states, or pulmonary oedema. The risk of dilution states is inversely proportional to the electrolyte concentrations of the injections. The risk of solute overload causing congested states with peripheral and pulmonary oedema is directly proportional to the electrolyte concentrations of the injections.

Depending on the volume and rate of infusion and depending on a patient's underlying clinical condition and capability to metabolise glucose, intravenous administration of glucose can cause:

- hyperosmolality, osmotic diuresis and dehydration
- hypoosmolality
- electrolyte disturbances such as
  - hypo- or hyperosmotic hyponatraemia (see below)
  - hypokalaemia
  - hypophosphataemia
  - hypomagnesaemia
  - overhydration/hypervolaemia and, for example, congested states, including pulmonary congestion and oedema.

The above effects do not only result from the administration of electrolyte-free fluid but also from glucose administration. In addition:

- an increase in serum glucose concentration is associated with an increase in serum osmolality. Osmotic diuresis associated with hyperglycaemia can result in or contribute to the development of dehydration and in electrolyte losses
- hyperglycaemia also causes a transcellular shift of water, leading to a decrease in extracellular sodium concentrations and hyponatraemia
- since glucose is metabolised, infusion of glucose solution corresponds to increasing the body's load of free water, possibly leading to hypoosmotic hyponatraemia.

Monitoring of serum sodium is particularly important. High volume infusion must be used under specific monitoring in patients with cardiac or pulmonary failure, and in patients with non-osmotic vasopressin release (including SIADH), due to the risk of hospital-acquired hyponatraemia.

Acute hyponatraemia can lead to acute hyponatraemic encephalopathy (cerebral oedema) characterised by headache, nausea, seizures, lethargy and vomiting which can lead to coma and death. Patients with cerebral oedema are at particular risk of severe, irreversible and life-threatening brain injury. Acute symptomatic hyponatraemic encephalopathy is considered a medical emergency.

The risk for developing hypoosmotic hyponatraemia is increased, for example,
- in children
- in elderly patients
- in women
- postoperatively
- in persons with psychogenic polydipsia.

The risk for developing encephalopathy as a complication of hypoosmotic hyponatraemia is increased, for example,
- in paediatric patients (≤16 years of age)
- in women (in particular, premenopausal women)
- in patients with hypoxemia
- in patients with underlying central nervous system disease.

Clinical evaluation and periodic laboratory determinations may be necessary to monitor changes in fluid balance, electrolyte concentrations, and acid-base balance during prolonged parenteral therapy or whenever the condition of the patient or the rate of administration warrants such evaluation.

Particular caution is advised in patients at increased risk of and from water and electrolyte disturbances that could be aggravated by increased free water load. Hyperglycaemia or possibly required insulin administration (see **Hyperglycaemia** below).

Preventive and corrective measures must be instituted as clinically indicated.

Hyperglycaemia

As with the intravenous administration of nutrients (e.g. glucose, amino acids and lipids) in general, metabolic complications may occur if the nutrient intake is not adapted to the patient's requirements, or the metabolic capacity of any given dietary component is not accurately assessed. Adverse metabolic effects may arise from administration of inadequate or excessive nutrients or from inappropriate composition of an admixture for a particular patient's needs.

Rapid administration of glucose solutions may produce substantial hyperglycaemia and a hyperosmolar syndrome. In order to avoid hyperglycaemia the infusion rate should not exceed the patient's ability to utilise glucose. To reduce the risk of hyperglycaemia-associated complications, the infusion rate must be adjusted and/or insulin administered if blood glucose levels exceed levels considered acceptable for the individual patient.

Intravenous glucose solution should be administered with caution in patients with, for example:

- impaired glucose tolerance (such as in diabetes mellitus, renal impairment, or in the presence of sepsis, trauma, or shock)
- severe malnutrition (risk of precipitating a refeeding syndrome)
- water and electrolyte disturbances that could be aggravated by increased glucose and/or free water load.

Thiamine diphosphate, cocarboxylase, is an essential co-enzyme in the carbohydrate metabolism; therefore, patients having thiamine deficiency, e.g. in patients with chronic alcoholism (risk of severe lactic acidosis due to impaired oxidative metabolism of pyruvate), should be treated cautiously with glucose intravenous infusion.

The glucose injections should be used with caution in patients with overt or subclinical diabetes mellitus (see section 4.5 Interactions with other medicines and other forms of interactions).

Other groups of patients in whom glucose intravenous infusions should be used with caution include:

- patients with ischaemic stroke. Hyperglycaemia has been implicated in increasing cerebral ischaemic brain damage and impairing recovery after acute ischaemic strokes (see also section 4.3 Contraindications).
- patients with severe traumatic brain injury. Early hyperglycaemia has been associated with poor outcomes in patients with severe traumatic brain injury (see also section 4.3 Contraindications).
- newborns (see section 4.4 Special warnings and precautions for use, Paediatric use).

Prolonged intravenous administration of glucose and associated hyperglycaemia may result in decreased rates of glucose-stimulated insulin secretion.

Refeeding syndrome

Refeeding severely undernourished patients may result in the refeeding syndrome that is characterised by the shift of potassium, phosphorus, and magnesium intracellularly as the patient becomes anabolic. Thiamine deficiency and fluid retention may also develop. Careful monitoring and slowly increasing nutrient intakes while avoiding overfeeding can prevent these complications.

Catheter infection and sepsis

Infection and sepsis may occur as a result of the use of intravenous catheters to administer parenteral formulations, poor maintenance of catheters or contaminated solutions.

Immunosuppression and other factors such as hyperglycaemia, malnutrition and/or their underlying disease state may predispose patients to infectious complications.

Careful symptomatic and laboratory monitoring for fever/chills, leukocytosis, technical complications with the access device, and hyperglycaemia can help recognise early infections.

The occurrence of septic complications can be decreased with heightened emphasis on aseptic technique in catheter placement, maintenance, as well as aseptic technique in nutritional formula preparation.

Others

Clinical evaluation and periodic laboratory determinations are necessary to monitor changes in blood, urinary glucose, fluid balance, electrolyte concentrations and acid-base balance especially during prolonged parenteral therapy or whenever the condition of the patients warrants such evaluation.

Use in the elderly

When selecting the type of infusion solution and the volume/rate of infusion for a geriatric patient, consider that geriatric patients are generally more likely to have cardiac, renal, hepatic, and other diseases or concomitant drug therapy.

Paediatric use

The infusion rate and volume depends on the age, weight, clinical and metabolic conditions of the child and concomitant therapy. Only Consulting Physicians experienced in paediatric intravenous fluid therapy should determine glucose intravenous infusion rate and volume.

Hypo-/hyperglycaemia

Neonates, especially those born premature and with low birth weight, are at increased risk of developing hypo- or hyperglycaemia. Close monitoring during treatment with intravenous glucose solutions is needed to ensure adequate glycaemic control in order to avoid potential long term adverse effects. Hypoglycaemia in the neonate can cause prolonged seizures, coma and cerebral injury. Hyperglycaemia has been associated with cerebral injury (including intraventricular haemorrhage), late onset bacterial and fungal infection, retinopathy of prematurity, necrotising enterocolitis, increased oxygen requirements, bronchopulmonary dysplasia, prolonged length of hospital stay, and death.

Hyponatraemia

Children (including neonates and older children) are at increased risk of developing hypoosmotic hyponatraemia as well as for developing hyponatraemic encephalopathy. Acute hyponatraemia can lead to acute hyponatraemic encephalopathy (cerebral oedema) characterised by headache, nausea, seizures, lethargy and vomiting which can lead to coma and death. Patients with cerebral oedema are at particular risk of severe, irreversible and life-threatening brain injury. Acute symptomatic hyponatraemic encephalopathy is considered a medical emergency.

Plasma electrolyte concentrations should be closely monitored in the paediatric population. Rapid correction of hypoosmotic hyponatraemia is potentially dangerous (risk of serious neurologic complications). Dosage, rate, and duration of administration should be determined by a physician experienced in paediatric intravenous fluid therapy.

Caution should be taken when used in infants with diabetic mothers.

Effects on laboratory tests

No data available.

4.5 Interactions with other medicines and other forms of interactions

Glucose solutions should not be administered concomitantly with blood through the same infusion set, as haemolysis and clumping may occur.

Both the glycaemic effects of Glucose Intravenous Infusion BP 5% and its effects on water and electrolyte balance should be taken into account in patients treated with other substances that affect glycaemic control, or fluid and/or electrolyte balance. Use of these glucose infusions may necessitate review of a patient's oral hypoglycaemic or insulin requirements, so close monitoring of serum glucose levels is required.

Caution is advised when administering Glucose Intravenous Infusion BP 5% to patients treated with drugs leading to an increased vasopressin effect. The below listed drugs increase the vasopressin effect, leading to reduced renal electrolyte free water excretion and may increase the risk of hyponatraemia following treatment with IV fluids. (See section 4.4 Special warnings and precautions for use and section 4.8 Adverse effects (undesirable effects)).

- Drugs stimulating vasopressin release such as chlorpropamide, clofibrate, carbamazepine, vincristine, selective serotonin reuptake inhibitors (SSRIs), 3.4-methylenedioxy-N- methamphetamine, ifosfamide, antipsycotics, opioids.
- Drugs potentiating vasopressin action such as chlorpropamide, non-steroidal antiinflammatories (NSAIDS), cyclophosphamide.
- Vasopressin analogues such as desmopressin, oxytocin, vasopressin, terlipressin.

Caution is advised when administering glucose infusions to patients treated with drugs that may increase the risk of hyponatraemia, such as diuretics and antiepileptics (e.g., oxcarbazepine).

See section 6.2 Incompatibilities.

4.6 Fertility, pregnancy and lactation

Effects on fertility

No data available.

Use in pregnancy – Pregnancy Category B3

Safety in pregnancy has not been established. Animal reproduction studies have not been conducted with Glucose Intravenous Infusion BP 5%. It is also not known whether Glucose Intravenous Infusion BP 5% causes fetal harm when administered to a pregnant woman or can affect reproduction capacity. Intrapartum maternal intravenous glucose infusion may result in fetal insulin production, with an associated risk of fetal hyperglycaemia and metabolic acidosis as well as rebound hypoglycaemia in the neonate. Glucose Intravenous Infusion BP 5% should be used during pregnancy only when clearly needed and the benefits of therapy outweigh the potential risks.

Use in lactation

Safety in lactation has not been established. Use Glucose Intravenous Infusion BP 5% in nursing woman only when clearly needed and the potential benefits outweigh the potential risks to the baby.

4.7 Effects on ability to drive and use machines

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 Adverse effects (undesirable effects)

- Infusion of glucose at a rate greater than 0.5 g/kg/hr may cause hyperglycaemia and glycosuria, if undetected and untreated, this can lead to diuresis, dehydration, hyperosmolar coma, and death. Continual clinical monitoring is recommended (see section 4.4 Special warnings and precautions for use). Rapid infusion of 25 - 50 g over 3 minutes may occasionally cause a generalised flush which usually subsides within 10 minutes.

- Oedema, hypokalaemia, hypophosphataemia and hypomagnesaemia. The utilisation of glucose will cause the intracellular movement of phosphate and potassium; in certain conditions provision must be made for replacing these products.

- Dilute electrolyte concentrations and disrupted fluid and acid-base balance with prolonged use.

- Hyperglycaemia and dehydration have resulted from inappropriate parenteral use. If administered to diabetic patients, insulin requirements may be modified (see section 4.5 Interactions with other medicines and other forms of interactions).

- Vitamin B complex deficiency. The administration of glucose without adequate provision of certain B vitamins, which form the coenzyme systems in its metabolism, will exhaust tissue stores of these factors, leading to deficiency states. This is particularly important in alcoholics when subclinical thiamine deficiency may precipitate an overt deficiency syndrome such as Wernicke's encephalopathy.

- Reactions that may occur because of the solution (e.g. from contamination), additive drugs or techniques of administration include fever response (due to possible introduction of pyrogens), infection at the site of injection, venous thrombosis or phlebitis extending from the site of injection, extravasation and hypervolemia. In case of such adverse reactions, the infusion should be stopped. Thrombophlebitis may result from the use of hypertonic solutions via the intravenous route.

- Anaphylactoid effects have been reported in two patients with both asthma and diabetes mellitus.

- Glucose administration can exacerbate diabetes mellitus.

- If an adverse reaction does occur, discontinue the infusion, evaluate the patient, institute appropriate therapeutic countermeasures and save the remainder of the fluid for examination if deemed necessary. The nature of any additives should be considered in the event of other undesirable effects.

Post-marketing adverse reactions

The following adverse reactions have been reported in the post-marketing experience, listed by MedDRA System Organ Class (SOC), then where feasible, by Preferred Term in order of severity.

- IMMUNE SYSTEM DISORDERS: hypersensitivity/infusion reactions including, anaphylactic/anaphylactoid reactions, including reactions with mild manifestations, e.g. pruritus, and reactions with severe manifestations, e.g. bronchospasm, cyanosis, angioedema and hypotension, pyrexia, chills.
- METABOLISM AND NUTRITION DISORDERS: hyperglycaemia.
- VASCULAR DISORDERS: phlebitis.
- SKIN AND SUBCUTANEOUS TISSUE DISORDERS: rash.
- GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS: infusion site reactions, infusion site phlebitis, infusion site erythema.

Other adverse reactions (Class reactions)

Other adverse reactions reported with other similar products include:

- hyponatraemia (which may be symptomatic)
- hyponatraemic encephalopathy.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 Overdose

Excessive administration of Glucose Intravenous Infusion BP 5% can cause hyperglycaemia, adverse effects on water and electrolyte balance, and corresponding complications (see section 4.4 Special warnings and precautions for use and 4.8 Adverse effects (undesirable effects)). For example, severe hyperglycaemia and severe dilutional hyponatraemia, and their complications, can be fatal. Clinically significant overdose of glucose intravenous infusion may, therefore, constitute a medical emergency.

Symptoms

Prolonged administration or rapid infusion of large volumes of isotonic solutions may cause oedema or water intoxication. Hyperglycaemia and glycosuria may occur, and if undetected can lead to mental confusion, dehydration, hyperosmolar coma and death.

The signs and symptoms of over infusion will also be related to the nature of any additive drugs.

Treatment

The infusion should be discontinued and the patient observed for appropriate signs and symptoms related to glucose and/or additive drugs administered, and appropriate symptomatic and supportive measures instituted as required, such as administration of insulin. Fluid overload and biochemical imbalance should be treated with corrective therapy. If diuresis is adequate, administration of a slightly hypotonic electrolyte solution in a quantity calculated to

replace the net quantity of fluid and specific electrolytes (particularly potassium) lost to osmodiuresis, whilst continuously monitoring serum electrolytes, fluid balance and acid-base status is recommended.

A suitable basic solution for replacing fluids and major electrolytes could be made up according to the following formulation per 1000 mL: Na+: approx. 120 mmol, K+: approx. 30 mmol, Cl-: approx. 150 mmol. Other electrolytes should also be replaced to make up for losses incurred.

In addition to replacement of net losses of fluids and electrolytes to diuresis, any acid-base imbalance should be corrected whilst continuing to monitor laboratory values.

In patients with oliguria or those with anuria, peritoneal dialysis or extracorporeal haemodialysis using carbohydrate-free solutions can be considered as a last resort.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Mechanism of action

Glucose is a naturally occurring monosaccharide found in the blood and is the principle source of energy for the body.

Glucose is metabolised in the body to carbon dioxide and water with the release of energy and calories.

It is stored in the body as fat and in the liver and muscles as glycogen. Glycogen is broken down and converted to glucose when body glucose level is depleted. As well as providing a source of energy, glucose infusions may reduce catabolic loss of nitrogen from the body and help prevent depletion of liver glycogen. It is also a source to be converted for nucleic acid formation.

Clinical trials

No data available.

5.2 Pharmacokinetic properties

No data available.

5.3 Preclinical safety data

Genotoxicity

The active ingredient, glucose, in Glucose Intravenous Infusion BP 5% is not a mutagen. It is a basic nutrient in all living cells.

Carcinogenicity

The active ingredient, glucose in Glucose Intravenous Infusion BP 5% is not carcinogenic. It is a basic nutrient in all living cells.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Sodium hydroxide (when necessary, for pH adjustment)
- Hydrochloric acid (when necessary, for pH adjustment)
- Water for injections

6.2 Incompatibilities

Additives may be incompatible. Consult with pharmacist, if available. Check the Product Information document(s) of the medication(s) and other relevant literature prior to their addition to Glucose Intravenous Infusion BP 5%. Complete information is not available. Those additives known to be incompatible should not be used.

Glucose Intravenous Infusion BP 5% should not be administered simultaneously with blood preparations through the same administration set, because of the possibility of pseudo-agglutination or haemolysis.

See section 4.4 – Special warnings and precautions for use and section 4.5 Interactions with other medicines and other forms of interactions.

6.3 Shelf life

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 Special precautions for storage

Store below 25 °C

Single use only. Discard unused portion.

6.5 Nature and contents of container

Glucose Intravenous Infusion BP 5% 100 mL Glass Vial.

Pack size: 100 mL x 10.

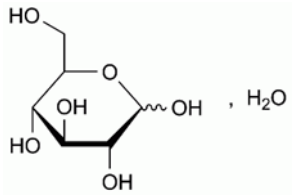
6.6 Special precautions for disposal

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 Physicochemical properties

Chemical structure

The molecular formula is $C_6H_{12}O_6.H_2O$ and the chemical structure is



CAS number

77938-63-7, 14431-43-7

7. MEDICINE SCHEDULE (POISONS STANDARD)

Unscheduled

8. SPONSOR

Pfizer Australia Pty Ltd
Level 17, 151 Clarence Street
Sydney NSW 2000
Toll Free Number: 1800 675 229
www.pfizer.com.au

9. DATE OF FIRST APPROVAL

31 July 2000

10. DATE OF REVISION

09 September 2021

Summary Table of Changes

Section changed	Summary of new information
4.1, 4.4, 4.6, 4.8, 6.5	Minor editorial changes: amend punctuation, corrections to text, include sub-headings, text relocation, align to PI format requirements.

4.3	Include patients with clinically significant hyperglycaemia, recent head trauma, hypersensitivity.
4.4	Included new sub-headings and text under Hypersensitivity reactions, Dilutions and other effects on serum electrolytes, Hyperglycaemia, Refeeding syndrome, Catheter infection and sepsis, Others. Additional information included under sub-headings Use in the elderly, Paediatric use – Hypo-/hyperglycaemia and – Hyponatraemia.
4.5	Included text regarding patients treated with other substances that affect glycaemic control or fluid and/or electrolyte balance, drugs leading to an increased vasopressin effect, drugs that may increase risk of hyponatraemia.
4.6	Additional clarification included under Use in pregnancy and Use in lactation.
4.8	Expand on adverse reactions caused by infusion at a rapid rate, and reactions that may occur because of the solution, additive drugs or techniques of administration. Include text relating to hyperglycaemia and dehydration. Include recommendations in event of an adverse reaction. Include new sub-headings and text under Post-marketing adverse reactions and Other adverse reactions (Class reactions).
4.9	Additional text included to expand on consequences of overdose. Information included to expand on corrective therapy.
5.3	Expand text under Genotoxicity and Carcinogenicity.
6.2	Expand text relating to additives and simultaneous administration with blood preparations.