AUSTRALIAN PRODUCT INFORMATION – DBL™ OCTREOTIDE INJECTION (Octreotide acetate) Solution for Injection

1. NAME OF THE MEDICINE

Octreotide acetate.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

DBL™ Octreotide Injection contains octreotide (as acetate), a synthetic octapeptide analogue of somatostatin.

Each 1 mL vial contains 0.05 mg, 0.1 mg or 0.5 mg octreotide (as acetate).

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

3. PHARMACEUTICAL FORM

Solution for injection.

DBL™ Octreotide Injection is a clear colourless solution free of foreign matter.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

- For symptomatic control and reduction of growth hormone and IGF-1 plasma levels in patients with acromegaly, including those who are inadequately controlled by surgery, radiotherapy or dopamine agonist treatment. Octreotide treatment is also indicated in acromegalic patients unfit or unwilling to undergo surgery, or in the interim period until radiotherapy becomes fully effective.

- For the relief of symptoms associated with the following functional tumours of the gastro-entero-pancreatic endocrine system:

    - Carcinoid tumours with features of the carcinoid syndrome

    - Vasoactive intestinal peptide secreting tumours (VIPomas).

  Octreotide is not an antitumour therapy and is not curative in these patients.

- For reduction of the incidence of complications following pancreatic surgery.

4.2 Dose and Method of Administration

Dosage

Acromegaly

Initially 0.05 to 0.1 mg by subcutaneous injection every 8 or 12 hours. Dosage adjustment should be based on monthly assessment of GH and IGF-1 levels (target: GH <2.5 ng/mL; IGF-1 within normal range) and on clinical symptoms and on tolerability. In most patients the optimal daily dose will be 0.2 to 0.3 mg. A maximum dose of 1.5 mg per day should not be exceeded. For patients on a stable dose of octreotide, assessment of biochemical markers should be made periodically.

If no relevant reduction of GH levels and no improvement of clinical symptoms have been achieved within three months of starting treatment with octreotide, therapy should be discontinued.

Gastro-entero-pancreatic endocrine tumours

Initially 0.05 mg once or twice daily by subcutaneous injection. Depending on clinical response, the effect on levels of circulating tumour products, and on tolerability, dosage can be gradually increased to 0.2 mg 3 times daily. Under exceptional circumstances higher doses may be required, however experience with doses above 750 µg per day is limited. Maintenance doses can be variable, depending on differences in tumour activity and rate of progression.

Complications following pancreatic surgery

0.1 mg three times daily by subcutaneous injection for seven consecutive days, starting on the day of operation at least one hour before laparotomy.

Method of Administration

Patients who are to self-administer the drug by subcutaneous injection must receive precise directions from the physician or the nurse.

To reduce local discomfort, it is recommended that the solution reaches room temperature before injection. Multiple injections at short intervals at the same site should be avoided. Vials should be opened just prior to administration and any unused portion discarded.

Parenteral drug products should be inspected visually for particulate matter and discolouration prior to administration. Do not use if particulates and/or discolouration are observed.

DBL™ Octreotide Injection contains no antimicrobial agent. Product is for single use in one patient only. Discard any remaining contents.

4.3 Contraindications

Hypersensitivity to octreotide or to any component of the formulation.

4.4 Special Warnings and Precautions for Use

Cardiovascular related events

Common cases of bradycardia have been reported. Medical review including dose adjustment of this agent and dose adjustments of drugs such as beta-blockers, calcium channel blockers, or agents to control fluid and electrolyte balance may be necessary.

Development of gallstones

Development of gallstones has been reported in 15 to 30% of long-term recipients of octreotide. The prevalence in the general population (aged 40 to 60 years) is estimated from reviews to be about 5 to 20%. Cholelithiasis is a very common event during octreotide treatment and may be associated with cholecystitis and biliary tract dilatation (see Section 4.8 Adverse Effects (Undesirable Effects)). Additionally, in the post-marketing setting, cases of cholangitis have been reported as a complication of cholelithiasis in patients receiving octreotide. Ultrasonic examination of the gallbladder before and at 6 to 12 monthly intervals during octreotide therapy is therefore recommended. If gallstones do occur, they are usually asymptomatic; symptomatic stones should be treated either by dissolution therapy with bile acids or by surgery.

GH secreting pituitary tumours

As GH secreting pituitary tumours may sometimes expand, thereby causing serious complications (e.g. visual field defects), it is essential that all patients be carefully monitored. If evidence of tumour expansion appears, alternative procedures may be advisable.

Gastro-entero-pancreatic endocrine tumours

In the treatment of gastro-entero-pancreatic endocrine tumours sudden escape from symptomatic control by octreotide may occur infrequently, with rapid recurrence of severe symptoms.

Effects on glucose regulation

In patients with concomitant hypersecretion of insulin, octreotide, because of its greater relative potency in inhibiting secretion of growth hormone and glucagon than of insulin, and its shorter duration of action on inhibition of the latter, may increase the depth of, and prolong the duration of hypoglycaemia. Such patients should be closely observed on introduction of octreotide therapy and at each change of dosage. Marked fluctuations of blood glucose concentration may possibly be reduced by more frequent administration of octreotide.

Patients with type I diabetes mellitus requiring insulin therapy may have their insulin requirements reduced by administration of octreotide. In non-diabetic patients and patients with type II diabetes mellitus who have partially intact insulin reserves, octreotide administration can result in prandial increases in glycaemia (see Section 4.8 Adverse Effects (Undesirable Effects)). It is therefore recommended to monitor glucose tolerance and antidiabetic treatment.

Oesophageal varices

Octreotide administration to patients who have concomitant bleeding gastro-oesophageal varices due to underlying hepatic cirrhosis increases the risk of development of insulin-dependent diabetes or of changes in insulin requirements in the presence of pre-existing diabetes. Therefore, appropriate monitoring of blood glucose levels is mandatory.

Nutrition

Octreotide may alter absorption of dietary fats in some patients.

Depressed vitamin B_{12} levels and abnormal Schilling's tests have been observed in some patients receiving ocreotide therapy. Monitoring of vitamin B_{12} levels is recommended during therapy with DBL™ Octreotide Injection in patients who have a history of vitamin B_{12} deprivation.

Thyroid function

Thyroid function should be monitored in patients receiving prolonged treatment with octreotide.

Use in hepatic impairment

In patients with liver cirrhosis, the half-life of the drug may be increased. If this occurs, adjustment of the maintenance dose may be considered.

Use in renal impairment

Impaired renal function did not affect the total exposure (AUC) to octreotide when administered subcutaneously. Therefore, no dose adjustment of octreotide is necessary.

Use in the elderly

In elderly patients treated with octreotide, there was no evidence for reduced tolerability or altered dosage requirements.

Paediatric use

Experience with octreotide in children is very limited.

Effects on laboratory tests

See subheading Nutrition above.

4.5 Interactions with Other Medicines and Other Forms of Interactions

Many patients with carcinoid syndrome or VIPomas being treated with octreotide have also been, or are being, treated with many other drugs to control the symptomatology or progression of the disease, including chemotherapeutic agents, H2 antagonists, antimotility agents, drugs affecting glycaemic states, solutions for electrolyte and fluid support or hyperalimentation, antihypertensive diuretics, and anti-diarrhoeal agents.

Octreotide has been reported to produce a reduction in the intestinal absorption of ciclosporin, and a delay in that of cimetidine.

Concomitant administration of octreotide and bromocriptine increases the bioavailability of bromocriptine.

Limited published data indicate that somatostatin analogs might decrease the metabolic clearance of compounds known to be metabolised by cytochrome P450 enzymes, possibly due to the suppression of growth hormone. Since it cannot be excluded that octreotide may have

this effect, other drugs which are mainly metabolised by CYP3A4 and which have a low therapeutic index (e.g. quinidine, terfenadine) should be used with caution.

Since octreotide has also been associated with alterations in nutrient absorption, its effect on absorption of any orally administered drugs should be carefully considered.

Where symptoms are severe and octreotide therapy is added to other therapies used to control glycaemic states such as sulphonylureas, insulin, diazoxide, and to beta blockers or agents for the control of fluid and electrolyte balance, patients must be monitored closely and adjustment made in the other therapies as the symptoms of the disease are controlled.

Evidence currently available suggests these imbalances in fluid and electrolytes or glycaemic states are secondary to correction of pre-existing abnormalities and not to a direct metabolic action of octreotide. Adjustment of the dosage of drugs, such as insulin, affecting glucose metabolism may be required following initiation of octreotide therapy in patients with diabetes (see Section 4.4 Special Warnings and Precautions for Use: Effects on glucose regulation).

4.6 Fertility, Pregnancy and Lactation

Women of childbearing potential

The therapeutic benefits of a reduction in growth hormone (GH) levels and normalisation of insulin-like growth factor 1 (IGF-1) concentration in female acromegalic patients could potentially restore fertility. Female patients of childbearing potential should be advised to use adequate contraception if necessary during treatment with octreotide.

Effects on fertility

It is not known whether octreotide has an effect on human fertility. Reproduction studies have been performed in rats and rabbits at doses up to 1 mg/kg octreotide and have revealed no evidence of any adverse effect of subcutaneous octreotide on fertility or morphogenesis (see Section 4.6 Fertility, Pregnancy and Lactation, subheading Use in Pregnancy below).Use in pregnancy – Pregnancy Category C

Category C: Drugs which, owing to their pharmacological effects, have caused or may be suspected of causing, harmful effects on the human foetus or neonate without causing malformations. These effects may be reversible.

No adequate and well controlled studies have been performed in pregnant women. In the post-marketing experience, data on a limited number of exposed pregnancies have been reported in patients with acromegaly, however, in half of the cases the pregnancy outcomes are unknown. Most women were exposed to octreotide during the first trimester of pregnancy at doses ranging from 100 to 300 µg/day of subcutaneous octreotide. In approximately two-thirds of the cases with known outcome, the women elected to continue octreotide therapy during their pregnancies. In most of the cases with known outcome, normal newborns were reported but also several spontaneous abortions during the first trimester, and a few induced abortions.

There were no cases of congenital anomalies or malformations due to octreotide usage in the cases that reported pregnancy outcomes.

DBL™ Octreotide Injection should only be prescribed to pregnant women under compelling circumstances.

Reproduction studies have been performed in rats and rabbits at doses up to 1 mg/kg and have revealed no evidence of any adverse effect of octreotide on fertility or morphogenesis. Fetal and post-natal growth retardation was seen in rats, probably due to suppression of growth hormone.

Use in lactation

It is not known whether octreotide is excreted in human breast milk. Animal studies have shown excretion of octreotide in breast milk. Patients should not breast-feed during treatment with DBL™ Octreotide Injection.

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.

However, adverse effects of this medicine include dizziness and asthenia which could affect the ability to drive or operate machinery (see Section 4.8 Adverse Effects (Undesirable Effects)).

4.8 Adverse Effects (Undesirable Effects)

The most frequent adverse reactions reported during octreotide therapy include gastrointestinal disorders, nervous system disorders, hepatobiliary disorders, and metabolism and nutritional disorders.

The most commonly reported adverse reactions in clinical trials with octreotide administration were diarrhoea, abdominal pain, nausea, flatulaence, headache, cholelithiasis, hyperglycaemia and constipation. Other commonly reported adverse reactions were dizziness, localised pain, biliary sludge, thyroid dysfunction (e.g. decreased thyroid stimulating hormone [TSH], decreased Total T4, and decreased Free T4), loose stools, impaired glucose tolerance, vomiting, asthenia, and hypoglycaemia.Adverse drug reactions accumulated from clinical studies with octreotide (see Table 1) are listed by the MedDRA system organ class (SOC). Within each SOC, the adverse drug reactions are ranked by frequency, with the most frequent first, using the following convention: *very common (≥ 1/10); common (≥ 1/100, < 1/10); uncommon (≥ 1/1,000, <1/100); rare (≥ 1/10,000, <1/1,000); very rare (< 1/10,000),* including isolated reports. Within each frequency grouping, adverse reactions are ranked in order of decreasing seriousness.

Table 1 Adverse drug reactions reported in clinical studies

Gastrointestinal disorders	
Very common:	Diarrhoea, abdominal pain, nausea, constipation, flatulence.
Common:	Dyspepsia, vomiting, abdominal bloating, steatorrhoea, loose stools, discolouration of faeces.
Nervous system disorders	
Very common:	Headache.
Common:	Dizziness.
Endocrine disorders	
Common:	Hypothyroidism, thyroid disorder (e.g. decreased TSH, decreased Total T4, and decreased Free T4).
Hepatobiliary disorders	
Very common:	Cholelithiasis.

Common:	Cholecystitis, biliary sludge, hyperbilirubinaemia.
Metabolism and nutrition disorders*	
Very common:	Hyperglycaemia
Common:	Hypoglycaemia, impaired glucose tolerance, anorexia.
Uncommon:	Dehydration.
General disorders and administration site conditions	
Very common:	Injection site reactions.
Common:	Asthenia.
Investigations	
Common:	Elevated transaminase levels.
Skin and subcutaneous tissue disorders	
Common:	Pruritus, rash, alopecia.
Respiratory disorders	
Common:	Dyspnoea.
Cardiac disorders	
Common:	Bradycardia.
Uncommon:	Tachycardia.

* Because of its inhibitory action on growth hormone, glucagon and insulin release, octreotide may affect glucose regulation and impair post-prandial glucose tolerance. In some instances, with chronic administration, a state of persistent hyperglycaemia may be induced. Hypoglycaemia has also been reported.

Flushing and oedema, events attributable to the underlying conditions, have been observed.

Post-marketing experience

Adverse drug reactions derived from post-marketing experience with octreotide via spontaneous case reports and literature cases are presented in Table 2. Because these reactions are reported voluntarily from a population of uncertain size it is not possible to reliably estimate frequency. Adverse drug reactions are listed according to SOCs in MedDRA, and are ranked in order of decreasing seriousness within each SOC.

Table 2 Adverse drug reactions derived from spontaneous reports and literature (frequency not known)

Blood and lymphatic system disorders	Thrombocytopenia
Immune disorders	Anaphylactic reaction, allergy/hypersensitivity reactions.
Skin and subcutaneous tissue disorders	Urticaria
Hepatobiliary disorders	Acute pancreatitis, acute hepatitis without cholestasis*, hepatitis cholestatic, cholestasis, jaundice, jaundice cholestatic.
Cardiac disorders	Arrhythmias.
Investigations	Blood alkaline phosphatase increased, gamma glutamyl transferase increased.

* Where there has been normalisation of transaminase values on withdrawal of subcutaneous octreotide.

One case of clinical hypothyroidism has been reported in a patient who had received 1500 µg octreotide daily for 19 months.

Description of selected adverse drug reactions

Injection site reactions

Local reactions include pain, a sensation of stinging, tingling or burning at the site of injection, with redness, swelling, irritation and rash. They rarely last more than fifteen minutes. Local discomfort may be reduced by allowing the solution to reach room temperature before injection or by injecting a smaller volume using a more concentrated solution.

Gastrointestinal system

Although measured faecal fat excretion may increase, there is no evidence to date that long-term treatment with octreotide has lead to nutritional deficiency due to malabsorption. In rare instances, gastrointestinal side effects may resemble acute intestinal obstruction with progressive abdominal distension, severe epigastric pain, abdominal tenderness and guarding. Occurrence of gastrointestinal side effects may be reduced by avoiding meals around the time of octreotide administration, that is, by injecting between meals or on retiring to bed.

Gallbladder

Prolonged use of octreotide may result in gallstone formation (see Section 4.4 Special Warnings and Precautions for Use).

Cardiac disorders

Bradycardia is a common adverse reaction with somastatin analogues. In both acromegalic and carcinoid syndrome patients, arrhythmia and ECG changes such as QT prolongation, axis shifts, early repolarisation, low voltage, R/S transition, early R wave progression, and non-specific ST-T wave changes were observed. The relationship of these events to octreotide acetate is not established because many of these patients have underlying cardiac diseases (see section 4.4 Special Warnings and Precautions for Use).

Pancreatitis

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Acute pancreatitis has been reported in rare instances. Generally, the effect is seen within the first hours or days of octreotide treatment and resolves on withdrawal of the drug. In addition, pancreatitis may develop in patients on long-term octreotide treatment who develop gallstones.

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

No life-threatening reactions have been reported after acute overdosage. The maximum single dose so far given to an adult has been 1.0 mg by intravenous bolus injection. The observed signs and symptoms were a brief drop in heart rate, facial flushing, abdominal cramps, diarrhoea, an empty feeling in the stomach and nausea, which resolved within 24 hours of drug administration. One patient has been reported to have received an accidental overdosage of

octreotide by continuous infusion (0.25 mg per hour for 48 hours instead of 0.025 mg per hour). He experienced no side effects.

The management of overdosage is symptomatic.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia). In New Zealand, call 0800 764 766.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Somatostatin and analogues, ATC code: H01CB02.

Mechanism of action

Octreotide is a synthetic octapeptide analogue of naturally occurring somatostatin with similar pharmacological effects, but with a considerably prolonged duration of action. It inhibits the secretion of serotonin and the gastro-entero-pancreatic peptides: gastrin, vasoactive intestinal peptide, insulin, glucagon, secretin, motilin, and pancreatic polypeptide, and of growth hormone (GH). Octreotide, like somatostatin, decreases splanchnic blood flow.

In animals, octreotide is a more potent inhibitor of growth hormone, glucagon and insulin release than somatostatin with greater selectivity for GH- and glucagon-suppression.

In healthy subjects octreotide, like somatostatin, has been shown to inhibit:

- Release of growth hormone (GH) stimulated by arginine, exercise and insulin-induced hypoglycaemia
- Postprandial release of insulin, glucagon, gastrin, other peptides of the GEP system, and arginine-stimulated release of insulin and glucagon
- Thyrotropin releasing hormone (TRH) stimulated release of thyroid stimulating hormone (TSH).

Unlike somatostatin, octreotide inhibits GH secretion preferentially over insulin and its administration is not followed by rebound hypersecretion of hormones (i.e. GH in patients with acromegaly).

In patients with acromegaly (including those who have failed to respond to surgery, radiation or dopamine agonist treatment) octreotide lowers plasma levels of GH and Insulin-like Growth Factor-1/Somatomedin C (IGF-1). A reduction in plasma GH (by 50% or more) occurs in almost all patients, and a plasma GH < 5 ng/mL can be achieved in about half of the cases. Most patients with symptoms such as headache, skin and soft tissue swelling, hyperhidrosis, arthralgia, paraesthesia report a reduction in these symptoms. In patients with a large pituitary adenoma, octreotide treatment may result in some shrinkage of the tumour mass.

In patients with functional tumours of the gastro-entero-pancreatic endocrine system, octreotide, because of its diverse endocrine effects, modifies different clinical features. Clinical improvement and symptomatic benefit occur in patients who have severe symptoms

related to their tumours despite previous therapies which include surgery, hepatic artery embolisation and various chemotherapies, e.g. streptozotocin and 5-fluorouracil.

Effects of octreotide in the different tumour types are as follows:

- *Carcinoid tumours:* Administration of octreotide may result in improvement of symptoms, particularly of flushing episodes and severe diarrhoea. In some cases this is accompanied by a fall in plasma serotonin and reduced urinary excretion of 5-hydroxyindole acetic acid. In the event of no beneficial response to octreotide treatment, continuation of therapy beyond one week at the maximum tolerated dose is not recommended, although in non-responders no serious sustained adverse drug effects have been reported.

- *Vasoactive intestinal peptide secreting tumours (VIPomas):* The biochemical characteristic of these tumours is overproduction of vasoactive intestinal peptide (VIP). In most cases, administration of octreotide results in alleviation of the severe secretory diarrhoea typical of the condition, with consequent improvement in quality of life. This is accompanied by an improvement in associated electrolyte abnormalities, e.g. hypokalaemia, enabling enteral and parenteral fluid and electrolyte supplementation to be withdrawn. In some patients, computer tomography scanning suggests a slowing or arrest of progression of the tumour, or even tumour shrinkage, particularly of hepatic metastases. Clinical improvement is usually accompanied by a reduction in plasma VIP levels, which may fall into the normal reference range.

For patients undergoing pancreatic surgery, the peri- and post-operative administration of octreotide reduces the incidence of typical post-operative complications (e.g. pancreatic fistula, abscess and subsequent sepsis, post-operative acute pancreatitis).

A large multi-centre study in patients with acute bleeding due to gastric or duodenal ulcer showed no benefit of octreotide over placebo in the control of haemorrhage.

Clinical trials

No data available

5.2 Pharmacokinetic Properties

Absorption

After subcutaneous injection, octreotide is absorbed rapidly and completely from the injection site. Peak concentrations of 5.5 ng/mL (100 µg dose) were reached 0.4 hours after dosing. In a single dose study, the absolute bioavailability after subcutaneous administration was found to be significantly different for different doses, however the interindividual variability was large. Relative to an equivalent intravenous dose, the bioavailability of a subcutaneous dose was estimated to be 80 to 135%. This was established based on the respective plasma concentrations determined by a radioimmunoassay. Peak concentrations and area under the curve values were dose proportional both after subcutaneous or intravenous single doses up to 400 µg and with multiple doses of 200 µg t.i.d. (600 µg/day). Clearance was reduced by about 66% suggesting non-linear kinetics of the drug at daily doses of 600 µg/day as compared to 150 µg/day. The relative decrease in clearance with doses above 600 µg/day is not defined.

Distribution

The distribution of octreotide from plasma was rapid ($t_{½\alpha}$= 0.2 hours) and the volume of distribution after intravenous dosing was estimated to be 0.27 L/kg body weight. In blood, the distribution into the erythrocytes was found to be negligible and about 65% was bound in the plasma in a concentration-independent manner. Binding was mainly to lipoprotein and, to a lesser extent, to albumin.

Excretion

The elimination of octreotide from plasma had an apparent half-life of 1.5 hours compared with 1 to 3 minutes with the natural hormone. The duration of action of octreotide is variable but extends up to 12 hours depending upon the type of tumour. About 32% of the dose is excreted unchanged into the urine.

The elimination capacity may be reduced in patients with liver cirrhosis (see Section 4.4 Special Warnings and Precautions for Use: Use in patients with impaired hepatic function), but not in patients with fatty liver disease.

Effect of renal and hepatic dysfunction on pharmacokinetics:

Impaired renal function did not affect the total exposure (AUC) to octreotide administered as a subcutaneous injection. Therefore, no dose adjustment is necessary. In patients with severe renal failure requiring dialysis, clearance was reduced to about half that found in normal subjects (from approximately 10 L/h to 4.5 L/h).

5.3 Preclinical Safety Data

Genotoxicity

Carcinogenicity

In repeat dose toxicity studies in rats of 52 weeks duration and longer, predominantly in males, sarcomas were noted at the subcutaneous injection site of octreotide in an acidic vehicle and at a lower incidence with the acidic vehicle alone. These did not occur in a mouse carcinogenicity study, nor did hyperplastic or neoplastic lesions occur at the subcutaneous injection site in a 52 week dog toxicity study.

There have been no reports of tumour formation at the injection sites in patients treated for up to 15 years with octreotide. All information available at present indicates that the finding of injection site sarcomas in rats is species-specific and has no significance for the use of the drug in humans.

The 116 week rat carcinogenicity study also revealed uterine endometrial adenocarcinomas, their incidence reaching statistical significance at the highest dose of 1.25 mg/kg per day. The presence of endometritis coupled with the absence of corpora lutea, the reduction in mammary fibroadenomas, and the presence of uterine dilatation suggest that the uterine tumours were associated with estrogen dominance in the aged female rats which does not occur in humans.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Glacial acetic acid

Sodium acetate trihydrate

Sodium chloride

Water for injections

6.2 Incompatibilities

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

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 at 2°C to 8°C (Refrigerate. Do not freeze). Store in the original packaging in order to protect from light.

6.5 Nature and Contents of Container

DBL™ Octreotide Injection is available in glass (Type 1 coloured) vials; pack sizes:

0.05 mg/1 mL vial, 5 pack	AUST R 120734
0.1 mg/1 mL vial, 5 pack	AUST R 120735
0.5 mg/1 mL vial, 5 pack	AUST R 120736

Not all pack sizes may be marketed.

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

H-D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-L-threoninol.

MW: 1019.3 (free peptide).

CAS number

Octreotide acetate: 79517-01-4.

7. MEDICINE SCHEDULE (POISONS STANDARD)

Schedule 4

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

20 June 2008

10. DATE OF REVISION

22 March 2021

Summary table of changes

Section changed	Summary of new information
All	PI reformat/editorial changes
Section 2	Added excipients with known effect.
Section 4.2	Removed duplicated information on the use in the elderly and in children.
Section 4.4	Added information on cardiovascular related events, nutrition and thyroid function. Updated information on gallstones.
Section 4.6	Added information in relation to women of childbearing potential. Added a statement regarding the effect of octreotide on human fertility. Expanded information on the use in pregnancy.
Section 4.8	The most frequent adverse reactions are updated. Added a statement of the most common adverse reactions reported from clinical trials. Added a table of ADRs reported from clinical trials with octreotide ranked by frequency within the MedDRA SOC. ADRs derived from post-marketing experience are listed according to SOCs in MedDRA, ranked in order of decreasing seriousness within each SOC. Newly listed ADRs: dyspnoea, tachycardia, endocrine disorders, dehydration, elevated transaminase levels, arrhythmias, Blood alkaline phosphatase increased, gamma glutamyl transferase increased. Added information on cardiac disorders.
Section 5.1	Added pharmacotherapeutic group.
Section 6.4	Added recommendation to store in the original packaging in order to protect from light.