Tobra-day™
Tobramycin (as sulfate) 500 mg in 5 mL injection

NAME OF THE MEDICINE

Tobramycin

4-O-(3-Amino-3-deoxy-α-d-glucopyranosyl)-2-deoxy-6-O-(2,6-diamino-2,3,6-trideoxy-α-d-ribo-hexopyranosyl)-l-streptamine.

The molecular weight of the compound is 467.5 and the CAS registry number is 32986-56-4.

The molecular formula is C18 H37N5O9

Structural Formula:

```
H2N

O

O

O

HO

HO

NH2

NH2

NH2

HO

OH

NH2

```

DESCRIPTION

Tobra-day™ is a sterile, clear, straw to pale yellow coloured solution containing tobramycin sulfate equivalent to 100 mg/mL tobramycin base in water for injections. Sulfuric acid and sodium hydroxide may be added to adjust pH (3.5-6.0). The solution is preservative free.

Tobramycin sulfate is a water soluble antibiotic of the aminoglycoside group and is produced by Streptomyces tenebrarius.

PHARMACOLOGY

Pharmacokinetics

Absorption

Tobramycin is rapidly absorbed following intramuscular injection and peak serum concentrations occur between 30 and 90 minutes after injection. In adults with normal renal function a single intramuscular injection of 1 mg/kg body weight will produce maximum serum levels of approximately 4 micrograms/mL and are measurable for as long as eight hours. When tobramycin is administered by the intravenous route
over a period of one hour serum concentrations are similar to those obtained after intramuscular injection.

Tobramycin is poorly absorbed from the gastrointestinal tract.

**Distribution**

After parenteral administration tobramycin can be detected in tissues and body fluids such as sputum, peritoneal fluid, synovial fluid and abscess fluids. Concentrations in bile and stools are normally low suggesting minimal biliary excretion. Tobramycin has appeared in low concentration in the cerebrospinal fluid following parenteral administration, and the concentrations are dependent on dose, rate of penetration and degree of meningeal inflammation.

Patients with cystic fibrosis (CF) have both an increased volume of distribution and an increased renal clearance with aminoglycosides. This results in the need for much higher doses of tobramycin than the general population.

**Excretion**

Aminoglycosides do not appear to be metabolised and tobramycin is excreted almost exclusively by glomerular filtration. Renal clearance is similar to that of endogenous creatinine. Ultrafiltration studies demonstrate that practically no serum protein binding occurs. In patients with normal renal function up to 84% of the dose is recoverable from the urine in 8 hours and up to 93% in 24 hours. The serum half life is usually 2-3 hours in adults with normal renal function but in patients with impaired renal function a range from 5 to 70 hours has been reported.

**Pharmacokinetics in Cystic Fibrosis Patients**

Following intravenous injection of tobramycin (8 to 12 mg/kg) in glucose injection over 30 minutes, the peak plasma concentration achieved ranges from 30 to 50 mg/L and is obtained in about 30 minutes. There is negligible plasma protein binding. The half-life is approximately 2 to 3 hours in patients with normal renal function but may be shorter in young children with CF.

**Microbiology**

Tobramycin is usually active against most strains of the following organisms: Pseudomonas aeruginosa, Escherichia coli. Proteus species (indole-positive and indole negative) including Proteus mirabilis, Proteus morganii, Proteus rettgeri and Proteus vulgaris Klebsiella, Enterobacter, Serratia species; Providencia species and Citrobacter species; Staphylococci, including Staphylococci aureus (coagulase positive and coagulase negative).

Aminoglycosides have a low order of activity against most Gram positive organisms; Enterococci and Streptococci are insensitive.

Aminoglycosides exhibit synergy with antibiotics, such as beta-lactams and vancomycin, which affect the bacterial cell wall and enhance aminoglycoside penetration. In vitro studies have shown that an aminoglycoside combined with an antibiotic that interferes with cell wall synthesis affects some group D streptococcal
strains synergistically. The combination of benzylpenicillin and tobramycin results in a synergistic bactericidal effect in vitro against certain strains of S. faecalis. However, this combination is not synergistic against other closely related organisms, e.g. S. faecium. Speciation of group D Streptococci alone cannot, therefore, be used to predict susceptibility. Susceptibility testing and tests for antibiotic synergism are recommended.

Anaerobic organisms, yeasts and fungi are resistant to aminoglycosides.

Cross resistance between aminoglycosides occurs and depends largely on inactivation by bacterial enzymes.

Bacterial resistance to tobramycin may occur and cross resistance between aminoglycosides may exist.

Bactericidal activity of aminoglycosides is concentration dependent. This activity is maximized when the serum peak concentration is between 8 and 10 times the MIC. The higher serum concentration of tobramycin with once-daily dosing increases the concentration-dependent killing of bacteria.

**CLINICAL TRIALS**

A large multicentre, randomised, double-blinded, comparative study assessed the safety and efficacy of once daily versus thrice daily tobramycin in CF patients with chronic pseudomonas aeruginosa infections. The primary endpoint was change in forced expiry volume in 1 second (FEV1) during 14 days treatment. A number of safety parameters, including serum creatinine and pure tone audiometry were assessed as secondary end points. A total of 244 patients from CF centres in the UK were randomly assigned to once or thrice daily tobramycin (with ceftazidime) for 14 days. 219 completed the treatment. Equivalence was demonstrated for the primary endpoint.

**INDICATIONS**

Tobra-day™ is indicated for once daily intravenous use in the treatment of cystic fibrosis patients (>5 years old) with acute pulmonary exacerbations caused by susceptible organisms.

**CONTRAINDICATIONS**

A hypersensitivity to any aminoglycoside is a contraindication to the use of tobramycin. A history of hypersensitivity or serious toxic reaction to any aminoglycoside may also contraindicate the use of any other aminoglycoside because of the known cross-sensitivity of patients to drugs in this class.

**PRECAUTIONS**

- Patients with :
  - Abnormal renal function prior to commencement of treatment with Tobra-day™
• Signs of diminishing renal function whilst undergoing treatment with once-daily Tobra-day™
• A history of abnormal renal function
• Dehydration

• Concurrent use with the following drugs:
  • Potent diuretics such as ethacrynic acid or frusemide
  • Other aminoglycosides (especially gentamicin)
  • Certain cephalosporins
  • Polymyxin B, colistin
  • Cisplatin, vancomycin
  • Ibuprofen
  • Amphotericin B
  • Methoxyflurane

• Patients with previous vestibular or auditory toxicity due to tobramycin or other aminoglycosides.
• Patients with existing vestibular or auditory dysfunction prior to initiation of Tobra-day™ therapy
• Patients who develop signs of ototoxicity during treatment with Tobra-day™.

Nephrotoxicity and ototoxicity: As with other aminoglycosides, patients treated with Tobra-day™ should be kept under close clinical observation because of its inherent potential to cause ototoxicity and nephrotoxicity.

Ototoxicity: Tobramycin is prone to cause eighth cranial nerve damage; both vestibular and auditory ototoxicity may occur with high, prolonged, set levels of the drug. The auditory changes are usually irreversible, usually bilateral and may be partial or total. The risk of aminoglycoside induced hearing loss increases with the degree of exposure to either high peak or high trough serum concentrations.

During therapy, some patients who develop cochlear damage may not show symptoms that warn of eighth cranial nerve damage, and partial or total bilateral damage may continue to develop even after therapy has been discontinued; therefore eighth nerve function should be carefully and regularly monitored in all patients. Serial audiograms should be obtained in patients that are old enough to be tested. Other manifestations of neurotoxicity include numbness, skin tingling, muscle twitching and convulsions.

Patients should be regularly asked about any hearing or balance problems and told to report such immediately if they occur. It is recommended that CF patients receiving Tobra-day™ should undergo routine audiometric testing. High frequency hearing loss precedes hearing loss across speech frequencies 5.

Tobra-day™ should be immediately discontinued if any sign of ototoxicity is noticed during routine monitoring.

Nephrotoxicity: Renal function should be closely monitored, and the drug discontinued in patients who develop signs of dysfunction during therapy. Tobramycin is selectively concentrated in renal cortical cells and it produces changes in proximal tubules. The drug causes renal impairment characterised by excretion of casts, oliguria, proteinuria and a progressive rise in blood urea and serum creatinine values.
Serum creatinine and creatinine clearance, serum calcium, magnesium, potassium, sodium levels and blood urea nitrogen should also be monitored. For urine, specific gravity and excretion of protein, cells and casts should be observed.

Serum creatinine should be checked, and creatinine clearance calculated (modified Cockcroft-Gault formula as recommended by Australian Therapeutic Guidelines: Antibiotics, Appendix 6) before commencing on Tobra-day™ and then 2 to 3 times each week or more frequently if renal function is very unstable.

Aminoglycoside induced nephrotoxicity is usually reversible. Rarely, nephrotoxicity may not manifest until the first few days after cessation of therapy.

*Use in impaired renal, vestibular and/or auditory function:* Evidence of impairment in renal, vestibular and/or auditory function requires discontinuation of the drug or at least reduction in dose if continuation of therapy is considered essential.

In high risk patients, the serum concentration of tobramycin should be monitored closely. Rising trough levels above 2 microgram/mL may indicate accumulation of the drug in tissues. It is this accumulation, high peak concentrations, dehydration and cumulative doses which may contribute to ototoxicity and nephrotoxicity. Ototoxicity may occur with peak levels lower than 12 microgram/mL.

*Neurologic and muscular disorders:* Aminoglycosides should be used with caution in patients suffering from muscular disorders such as myasthenia gravis or parkinsonism, as these drugs may aggravate muscle weakness because of their potential curare-like effect on neuromuscular function.

*Allergic reactions:* Administration of tobramycin may result in allergic reaction. Cross allergenicity among aminoglycosides has also been known to occur.

*Nonsusceptible organisms:* Therapy with tobramycin may result in overgrowth of nonsusceptible organisms. If overgrowth of nonsusceptible organisms occurs, appropriate therapy should be initiated.

*Effect on Fertility*

Tobramycin doses as great as 100 mg/kg when administered subcutaneously to rats had no adverse effects on fertility or reproduction. Daily subcutaneous administration of tobramycin doses of 20-40 mg/kg to pregnant rabbits caused anorexia, weight loss and renal injury. Fifteen percent of the animals of the 20 mg/kg group and 85 percent of those of the 40 mg/kg group died or aborted. Fetal development appeared normal in these animals at the time of death or abortion. No drug-related abnormalities were noted in any of the progeny, despite the maternal toxicity.

*Use in Pregnancy*

Category D

Aminoglycosides can cause fetal damage when administered during pregnancy. Aminoglycoside antibiotics cross the placenta and there have been reports of total irreversible bilateral congenital deafness in children whose mothers have received streptomycin or kanamycin during pregnancy. Tobramycin crosses the placenta,
distributes to most fetal tissues, and concentrates in fetal kidneys and urine. There have been no reports of teratogenicity after the use of tobramycin in humans although high doses have been reported to cause renal toxicity in pregnant rats, their fetuses and their newborns. Ototoxicity has not been reported as an effect of in utero exposure 5.

However, in view of the theoretical risks of aminoglycosides Tobra-day™ should only be used in pregnancy if the potential benefit outweighs the potential risk to the fetus.

Category D definition: Drugs which have caused, are suspected to have caused, or may be expected to cause an increased incidence of human fetal malformations or irreversible damage. These drugs may also have adverse pharmacological effects. Accompanying texts should be consulted for further details.

**Use in Lactation**

Tobramycin is excreted in the breast milk with concentrations of 0.60 and 0.85 micrograms /mL at one and eight hours after an intramuscular dose of 80 mg. Because of the potential to the newborn it is recommended that breast feeding be discontinued during therapy with Tobra-day™.

**Paediatric Use**

The use of once daily tobramycin in CF patients less than 5 years of age has not been studied. The indication for Tobra-day™ excludes children younger than 5 years of age.

**Use in Burns Patients**

In patients with extensive burns, pharmacokinetics may be altered resulting in reduced serum levels of tobramycin. Dosage should therefore be based on measured serum levels in these patients.

**Use During Anaesthesia**

Neuromuscular blockade and respiratory paralysis have been reported in cats receiving very high doses of tobramycin (40 mg/kg). The possibility of prolonged or secondary aponea should be considered if the drug is administered to anaesthetised patients who are concurrently receiving neuromuscular blocking agents such as suxamethonium, tubocurarine, or decethonium. This also applies to patients receiving massive transfusions of citrated blood. If neuromuscular blockade occurs, it may be reversed by the administration of calcium salts.

**Genotoxicity**

Tobramycin was found to be negative in the mouse lymphoma forward mutation assay. Tobramycin did not induce chromosomal aberrations in Chinese hamster ovary cells, and was negative in the mouse micronucleus test.
**Carcinogenicity**

Long term animal studies have not been performed to evaluate the carcinogenic potential of tobramycin by the intravenous route.

**INTERACTIONS WITH OTHER MEDICINES**

**Contraindicated Drugs**

Potent diuretics: do not give tobramycin in conjunction with ethacrynic acid, frusemide or other potent diuretics which may themselves cause ototoxicity or enhance aminoglycoside toxicity by altering antibiotic concentrations in serum and tissue.

Other neurotoxic and/or nephrotoxic agents: avoid concurrent or sequential use of other neurotoxic and/or nephrotoxic antibiotics, particularly other aminoglycosides, polymyxin B, colistin, cisplatin and vancomycin, ibuprofen 5.

Neuromuscular blocking agents or other medications with neuromuscular blocking activity: Care is required if other drugs with a neuromuscular blocking action are given concomitantly with aminoglycosides. The neuromuscular blocking properties of aminoglycosides may be sufficient to provoke severe respiratory depression in patients receiving general anaesthetics or opioids.

Amphotericin B: May produce synergistic renal toxicity.

Methoxyflurane: May produce additive or synergistic nephrotoxicity. Renal impairment may appear at lower than usual dosage levels of the drug.

**Care with use**

Neuromuscular blocking agents or other medication with neuromuscular blocking activity: Care is required if other drugs with a neuromuscular blocking action are given concomitantly with aminoglycosides. The neuromuscular blocking properties of aminoglycosides may be sufficient to provoke severe respiratory depression in patients receiving general anaesthetics or opioids. (See also Use During Anaesthesia)

Beta lactam antibiotics: Since aminoglycosides have been shown to be incompatible with some beta lactams in vitro, these antibiotics should be administered separately if both are required. Antagonism in vivo has been reported only in a few patients with severe renal impairment, in whom aminoglycoside activity was diminished.

**Incompatibilities**

Tobramycin injections have been reported to be incompatible with the solutions of the following: alcohol 5%, cefamandole nafate, cefepime HCl, flucloxacillin sodium, heparin sodium, propofol, clindamycin 8.

It is recommended that Tobra-day™ not be mixed with other drugs.
In addition, the activity of tobramycin appears to be inhibited by calcium and magnesium ions.

**ADVERSE EFFECTS**

Frequency estimate: very common≥10%; common≥1% to <10%; uncommon≥0.1% to <1%; rare ≥0.01% to<0.1%; very rare <0.01%

Table 1: Adverse drug reactions reported in clinical studies with CF patients.

**Ototoxic**

Common: high frequency hearing loss  
Uncommon: tinnitus

**Vestibular**

Common: acute dizziness, vertigo

**Renal and urinary disorders**

Very common: reduced creatinine clearance indicating reduced renal function  
Uncommon: increase in serum creatinine  
Rare: interstitial nephritis  
Rare: acute renal failure

**Immune system disorders**

Rare: respiratory depression  
Rare: rash  
Rare: anaphylaxis

As with other aminoglycosides, ototoxicity and nephrotoxicity can occur. The risk of adverse effects is increased in patients with poor renal function, the elderly, patients on prolonged treatment or with serious underlying pathology.

**More common adverse reactions.** Otic: Ototoxicity occurs as the drug penetrates into the inner ear during periods of high serum concentration. Both auditory and vestibular branches of the eighth cranial nerve may be adversely affected. Ototoxicity initially manifests as vestibular dysfunction with or without loss of high tone activity, similar to that of other aminoglycosides. Symptoms include dizziness, vertigo, tinnitus, roaring in the ears and hearing loss. Hearing loss is usually irreversible. Ototoxic damage may progress in some patients even after the drug is discontinued.

Renal: Nephrotoxicity: Reversible nephrotoxicity may occur and acute renal toxicity and interstitial nephritis have been reported often in association with other drugs which are nephrotoxic. (See Contraindications and Interactions with other
medicines). Decreased glomerular filtration is usually seen only after several days and may even occur after therapy has been stopped. Renal failure characterized by elevated creatinine and urea concentrations appears to be a rare complication of aminoglycoside therapy in patients with CF.

Patients with pre-existing renal impairment who are treated for longer periods or with higher doses than those recommended are at greater risk. Repeated intravenous aminoglycoside use in CF is associated with long term renal damage.

Nephrotoxicity manifests as changes in renal function: rising serum urea, blood urea nitrogen (BUN), nonprotein nitrogen (NPN) and serum creatinine and by oliguria, cylindruria and increased proteinuria. Nephrotoxicity may be increased by the concurrent administration of other drugs (see Contraindications and Interactions with other medicines). Patients with pre-existing renal impairment are at greatest risk. Adverse renal effects can occur in patients with initially normal renal function.

Gastrointestinal: Nausea, vomiting and diarrhoea.

**Less common reactions.** Musculoskeletal: The aminoglycosides are known to possess neuromuscular blocking effects and to be capable of exacerbating impairment of neuromuscular transmission in clinical conditions such as myasthenia gravis or severe hypocalcaemia, or when used in conjunction with nondepolarising neuromuscular relaxants such as d-tubocurarine.

Neuromuscular blockade may result in weakness of skeletal muscles and respiratory depression especially in patients with myasthenia gravis, severe hypocalcaemia or who have recently received other neuromuscular blocking agents. Peritoneal lavage with tobramycin could precipitate apnoea because high concentrations of drug come in contact with the diaphragm. Rarely, blockade has been observed following intramuscular or intravenous injection. Tobramycin is usually safely used prior to surgery if given in recommended single doses.

Dermatological: Maculopapular rash, urticaria, itching.

**Rare reactions.** Biochemical abnormalities: Some patients with malignant diseases have developed a complex metabolic syndrome of two to eight weeks duration after administration of tobramycin, including hypocalcaemia, hypomagnesaemia, hypokalaemia, hyperalbuminaemia, hypophosphataemia and hypouricaemia. Other reported abnormalities include increased AST, ALT, serum bilirubin and alkaline phosphatase.

Haematological and reticuloendothelial: Anaemia, granulocytopenia and thrombocytopenia, eosinophilia, decreased platelet and white cell counts.

Immunological: Fever, rash, itching, urticaria. Adverse effects on the immune response via inhibition of chemotaxis and microbicidal activity of phagocytes have been reported. Angioedema, exfoliative dermatitis, stomatitis and anaphylaxis are hypersensitivity reactions reported with aminoglycosides in general.

Neurological: Lethargy. Acute brain syndrome has been reported in an elderly patient after four days of therapy with tobramycin. The delirium was reversed after drug discontinuance. Neurotoxicity is rare with tobramycin. Peripheral neuropathy, paraesthesia and muscle weakness have been reported.
Other: Pain after intramuscular administration and thrombophlebitis after intravenous administration.

DOSAGE AND ADMINISTRATION

In patients with cystic fibrosis, the starting dose is 10 mg tobramycin per kg body weight per day. The dose is adjusted according to the results of therapeutic drug monitoring (TDM).

Initial dose selection (10 mg/kg/day) should be adjusted depending on renal function and previous patient experience. Further dose adjustment should take into account the results of therapeutic drug monitoring, renal function and audiometry testing.

The intravenous injection is diluted in a minimum volume of 50 mL of sodium chloride intravenous infusion (0.9% w/v) or 5% glucose intravenous infusion and infused over thirty to sixty minutes.

Once diluted the solution should be used as soon as possible. If storage is necessary the prepared solution should be refrigerated between 2°C and 8°C and stored for no longer than 24 hours before discarding.

Monitoring serum levels of tobramycin:

Monitoring of tobramycin plasma levels may be carried out by a number of methods using various nonograms and computer programs which use the area under curve method (Barclay et al)11. Traditional methods of monitoring for tobramycin toxicity using peak and trough levels are ineffective when giving tobramycin once a day (Coulthard et al)10. This is because higher peak levels will be achieved and trough levels are often unrecordable. The aim of TDM is to achieve adequate bactericidal effect with minimum toxicity as these patients will usually receive tobramycin for between 10 to 14 days, and in some cases longer.

The recommended method to achieve precise dosing and aid with dose adjustment is the use of a computer program for therapeutic drug monitoring accessed by a pharmacist.(Duffull et al)12.

Blood levels should be taken one hour and four to six hours post the first dose. Also required is the patient’s height, weight, age and serum creatinine. The dose, time of administration and the time blood levels were taken are also required for the calculation.

The following target levels can be used as a guide only:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cmax</td>
<td>&gt;20 mg/L</td>
</tr>
<tr>
<td>Cmin</td>
<td>&lt;0.5 mg/L</td>
</tr>
<tr>
<td>AUC</td>
<td>85-101 mg.h/L</td>
</tr>
</tbody>
</table>

If the dose is altered by more than 40 mg, blood levels should be repeated as above. If there is no alteration in dose, blood levels should be taken at least weekly for the duration of treatment.

Other monitoring recommendations to prevent toxicity include:
Regular serum creatinine levels to assess for renal toxicity at least weekly but more frequently if the patient is clinically unstable.

Otosotoxicity should be monitored using audiometry preferably at the end of each admission.

Tobra-day™ contains no antimicrobial agent and is for single use in one patient on one occasion only. Discard any residue.

Tobra-day™ and other antibiotics should be administered separately.

Further information

Further information concerning use of tobramycin in once-a-day regimens may be found in the AUSTRALIAN THERAPEUTIC GUIDELINES: ANTIBIOTIC 13th Ed. (2006) – AMINOGLYCOSIDES 6

OVERDOSAGE

Signs and symptoms: The severity of the signs and symptoms following a tobramycin overdose are dependent on the dose administered, the patient's renal function, state of hydration and age and whether or not other medications with similar toxicities are being administered concurrently. Neuromuscular blockade or respiratory paralysis may occur following administration of aminoglycosides. Nephrotoxicity, auditory and vestibular toxicity have been associated with aminoglycoside overdose.

Treatment: In managing overdose, consider the possibility of multiple drug overdoses, interaction among drugs, and unusual drug kinetics in the patient.

The initial intervention in a tobramycin overdose is to establish an airway and ensure oxygenation and ventilation. Resuscitative measures should be initiated promptly if respiratory paralysis occurs.

Patients that have received an overdose of tobramycin and have normal renal function should be adequately hydrated to maintain a urine output of 3 – 5 mL/kg/hr. Fluid balance, creatinine clearance, and tobramycin plasma levels should be carefully monitored.

Patients in whom the elimination half-life is greater than 2 hours or whose renal function is abnormal may require more aggressive therapy. In such patients, haemodialysis may be beneficial.

In Australia, contact the Poisons Information Centre on 13 11 26 for further advice on overdose management. In New Zealand, contact the Poisons Information Centre on 0800 POISON or 0800 764 766 for further advice on overdose management.

PRESENTATION AND STORAGE CONDITIONS

Tobra-day™ injection contains 500 mg tobramycin (as sulfate) in 5 mL water for injections. It also contains sulfuric acid and sodium hydroxide for pH adjustment. The
injection does not contain an antimicrobial preservative and is for use in one patient on one occasion only.

Store: Refrigerate 2°C-8°C. Do not freeze.

Protect from light.

Tobra-day™ injection is presented in a 7 mL amber glass vial containing 5 mL of solution as a pack of 10.

Phebra Product Code: INJ093

AUST R 150481

POISON SCHEDULE OF THE MEDICINE

Schedule 4 - Prescription only medicine

MEDICINE CLASSIFICATION (NEW ZEALAND)

Prescription medicine

NAME AND ADDRESS OF THE SPONSOR

Phebra Pty Ltd, 19 Orion Road, Lane Cove West, NSW 2066, Australia.
Telephone: 1800 720 020
Distributed in New Zealand by AFT Pharmaceuticals Ltd. PO Box 33-203 Auckland. Telephone: +64 9 4880232

DATE OF FIRST INCLUSION ON THE ARTG: 17TH July 2009
Date of Preparation (New Zealand): 19TH December 2013

REFERENCES

13. Tobra-day™, Phebra and Phi are trademarks of Phebra Pty Ltd, 332 Burns Bay Road, Lane Cove, NSW 2066, Australia.
14. Copyright, 2010, Phebra Pty Ltd, All rights reserved

Tobra-day, Phebra and the Phi symbol are trademarks of Phebra Pty Ltd, 332 Burns Bay19 Orion Road, Lane Cove West, NSW 2066, Australia.