Your medicine is available using the above name but will be referred to as Diamox Injection throughout this leaflet.

In this leaflet:
1. What Diamox Injection is and what it is used for
2. Before you are given Diamox Injection
3. How you are given Diamox Injection
4. Possible side effects
5. How to store Diamox Injection
6. Further information

1. WHAT DIAMOX INJECTION IS AND WHAT IT IS USED FOR
Diamox Injection contains the active substance Acetazolamide. This belongs to a group of medicines known as carbonic anhydrase inhibitors.

Diamox Injection is used to treat:
- glaucoma (a condition of the eye), by reducing the pressure within the eye.
- Fluid retention
- Some forms of epilepsy (“fits”), in combination with other anti-epileptic medicines to lower the sugar in your blood
- medicines to reduce blood pressure
- medicines for your heart such as cardiac glycosides (e.g. digoxin)
- a tingling or numbness in the fingers or toes, or coldness in the extremities
- feeling over-excited
- tiredness or irritability
- a need to pass urine more often than normal
- looking flushed
- a temporary short-sightedness which subsides when the dosage is reduced
- a loss of interest in sex
- feeling over-excited
- severe mental problems
- high or low blood sugar levels
- temporary short-sightedness which subsides when the dosage is reduced
- a tingling or numbness in the fingers or toes, or coldness in the extremities

2. BEFORE YOU ARE GIVEN DIAMOX INJECTION
You should NOT be given Diamox Injection if:
- you have low blood levels of sodium and/or potassium or high blood levels of chloride (your doctor will advise you)
- you have had chronic or congestive glaucoma (a condition of the eye), by reducing the pressure within the eye.
- you have, or have ever had severe kidney problems
- you have reduced function of the adrenal glands - glands above the kidneys - (also known as Addison's disease)
- you have low blood levels of sodium and/or potassium or high blood levels of chloride (your doctor will advise you)

Speak to your doctor if any of the above applies to you.

Take special care and speak to your doctor before taking Diamox Injection if:
- you have or have ever had kidney problems such as kidney stones
- you have lung problems such as chronic bronchitis or emphysema, which causes difficulty in breathing
- you have diabetes or problems with your blood sugar level
- You are over the age of 65
- You have, or have ever had severe liver problems
- You have, or have ever had severe kidney problems
- You have reduced function of the adrenal glands - glands above the kidneys - (also known as Addison's disease)
- You have low blood levels of sodium and/or potassium or high blood levels of chloride (your doctor will advise you)

Be prepared to monitor your blood to check that this does not happen. You might also experience bone thinning or the risk of kidney stones with long-term therapy.

3. HOW YOU ARE GIVEN DIAMOX INJECTION
Diamox Injection is a white powder which will be dissolved in water to make a solution for injection either into one of your veins (intravenous) or into one of your muscles (intramuscular).

4. POSSIBLE SIDE EFFECTS
All medicines can cause allergic reactions although serious allergic reactions are very rare. Any sudden wheeziness, difficulty in breathing, swelling of the eyelids, face or lips, rash or itching (especially affecting your whole body) should be reported to a doctor immediately.

Other side effects include:
- depression
- drowsiness or confusion
- a loss of interest in sex
- ringing in the ears or difficulty in hearing
- temporary short-sightedness which subsides when the dosage is reduced or treatment is stopped.

Rare cases of skin rashes including an increased sensitivity to sunlight have been reported. If you experience any unusual skin rashes, inform your doctor.

Very rarely, Diamox Injection can affect the liver and kidneys. If you experience pain in your lower back, pain or burning when you pass urine, have difficulty in passing urine, or you stop passing urine, have blood in your urine, pale stools, or if your skin or eyes look slightly yellow, you should contact your doctor. You should also contact your doctor if your stools are black or tarry, or if you notice blood in your stools.

If you are given Diamox Injection for a long time it can occasionally affect the amount of potassium, or sodium in your blood. Your doctor will probably take blood tests to check that this does not happen. You might also experience bone thinning or the risk of kidney stones with long-term therapy.

High or low blood sugar levels may occasionally occur.

Pregnancy and breast feeding:
Ask your doctor or pharmacist for advice before taking any medicines.

Diamox Injection SHOULD NOT be taken if you are pregnant, think you are pregnant or are planning to become pregnant. It may be taken when breast feeding but only on the advice of the doctor.

Driving and using machines:
If Diamox Injection makes you feel drowsy or confused you should not drive or operate machines. Diamox Injection can occasionally cause short-sightedness; if this happens and you feel that you can no longer drive safely, you should stop driving and contact your doctor.

Important information about some of the ingredients of Diamox Injection:
This medicine contains less than 1 mmol sodium (23mg) per dose, i.e. essentially “sodium-free”.

6. Further information
If any of the side effects becomes serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

Reporting of side effects:
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

By reporting side effects you can help provide more information on the safety of this medicine.

5. HOW TO STORE DIAMOX INJECTION
Keep out of the sight and reach of children.

Do not store above 25°C.
Any unused solution can be stored in a refrigerator for up to 24 hours but any unused solution after this period must be discarded.

Do not use after the expiry date. This date is printed on your pack. The Expiry date refers to last day of that month.

For single use only.

If the powder becomes discoloured or show any other signs of deterioration, consult your pharmacist who will tell you what to do.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION
What Diamox Injection Contains:
The active substance is acetazolamide.
Each vial contains 500mg acetazolamide (as acetazolamide sodium).

What Diamox Injection looks like and contents of the pack:
Diamox Injection is a white powder, packed in a transparent glass vial with a grey rubber stopper, aluminium ring seal and blue plastic plug. Before use, it is made into a solution, using at least 5ml water for injection.

Each carton contains 1 vial.

MANUFACTURER AND PRODUCT LICENCE HOLDER
Manufactured by Mercury Pharmaceuticals Ltd., Capital House, 85 King William Street, EC4N 7BL, London, UK.

BAG Health Care GmbH, Amttsrichsstrabe 1-5, D-35423 Lich, Germany.

Procured from within the EU by Product Licence holder:
Star Pharmaceuticals Ltd., 5 Sandridge Close, Harrow, Middlesex HA1 1XD. Repackaged by Servipharm Ltd.

Leaflet revision and issue date (Ref) 17.11.16[P-4]

Diamox is a trademark of Wyeth Holdings LLC.
1. NAME OF THE MEDICINAL PRODUCT
Diamox Sodium 500mg Powder for Solution for Injection.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each vial contains 500 mg acetazolamide (as acetazolamide sodium). For full list of excipients see section 6.1.

3. PHARMACEUTICAL FORM
White powder for solution for injection.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
Acetazolamide is an enzyme inhibitor which acts specifically on carbonic anhydrase. It is indicated in the treatment of:

i) Glaucoma: Diamox injection is useful in glaucoma (chronic simple (open angle) glaucoma, secondary glaucoma and peripherorally in acute angle closure glaucoma where delay of surgery is desired in order to lower intraocular pressure) because it acts on inflow, decreasing the amount of aqueous secretion.

ii) Abnormal retention of fluids: Diamox injection is a diuretic whose effect is due to the effect on the reversible hydration of carbon dioxide and dehydration of carbonic acid reaction in the kidney. The result is a renal loss of HCO3- ion which carries out sodium, water and potassium.

Diamox injection can be used in conjunction with other diuretics when effects on several segments of the nephron are desirable in the treatment of fluid retaining states.

iii) Epilepsy: In conjunction with other anticonvulsants best results with Diamox injection have been seen in petit mal in children. Good results, however, have been seen in patients, both children and adults, with other types of seizures such as grand mal, mixed seizure patterns, myoclonic jerk patterns, etc.

4.2 Posology and method of administration
Routes of Administration: Intravenous or intramuscular injection. The direct intravenous route is preferred as intramuscular use is limited by the alkaline pH of the solution.

i) Glaucoma (simple acute congestive and secondary):
Adults: 250-1000mg per 24 hours, usually in divided doses for amounts over 250mg daily.

ii) Abnormal retention of fluid: Congestive heart-failure, drug-induced oedema.
Adults: For diuresis, the starting dose is usually 250-375mg once daily in the morning. If, after an initial response, the patient fails to continue to lose oedema fluid, do not increase the dose but allow for kidney recovery by omitting a day. Best results are often obtained on a regime of 250-375mg daily for two days, rest a day, and repeat or merely giving Diamox injection every other day. The use of Diamox injection does not eliminate the need for other therapy, e.g. digitalis, bed rest and salt restriction in congestive heart failure and proper supplementation with elements such as potassium in drug-induced oedema. For cases of fluid retention associated with pre-menstrual tension, a daily dose (single) of 125-375mg is suggested.

ii) Epilepsy
Adults: 250-1000mg daily in divided doses.
Children: 8-10mg/kg in daily divided doses and not to exceed 750mg/day. The change from other medication to Diamox injection should be gradual. Elderly: Diamox injection should only be used with particular caution in elderly patients or those with potential obstruction in the urinary tract or with disorders rendering their electrolyte balance precarious or with liver dysfunction.

For reconstitution please refer to section to section 6.6 below

4.3 Contraindications
Diamox injection is contra-indicated in situations in which sodium and/or potassium blood levels are depressed, in cases of marked kidney and liver dysfunction, suprarenal gland failure and hyper-chloremic acidosis. Diamox injection should not be used in patients with hepatic cirrhosis as this may increase the risk of hepatic encephalopathy.

Long-term administration of Diamox injection is contra-indicated in patients with chronic non-congestive angle-closure glaucoma since it may permit organic closure of the angle to occur while the worsening glaucoma is masked by lower intraocular pressure.

Diamox injection should not be used in patients hypersensitive to sulphonamides.

4.4 Special warnings and special precautions for use
Suicidal ideation and behaviour have been reported in patients treated with antiepileptic agents in several indications. A meta-analysis of randomised placebo controlled trials of anti-epileptic drugs has also shown a small increased risk of suicidal ideation and behaviour. The mechanism of this risk is not known and the available data do not exclude the possibility of an increased risk for Diamox injection. Therefore patients should be monitored for signs of suicidal ideation and behaviours and appropriate treatment should be considered. Patients (and caregivers of patients) should be advised to seek medical advice should signs of suicidal ideation or behaviour emerge.

Increasing the dose does not increase the diuresis and may increase the incidence of drowsiness and/or paraesthesia.

Increasing the dose often results in a decrease in diuresis. Under certain circumstances, however, very large doses have been given in conjunction with other diuretics in order to secure diuresis in complete refractory failure. When Diamox injection is prescribed for long-term therapy, special precautions are advisable. The patient should be cautioned to report any unusual skin rash. Periodic blood cell counts and electrolyte levels are recommended. Fatalities have occurred, although rarely, due to severe reactions to sulphonamides. A precipitous drop in formed blood cell elements or the appearance of toxic skin manifestations should call for immediate cessation of Diamox injection therapy.

In patients with pulmonary oedema or emphysema where alveolar ventilation may be impaired, Diamox injection which may aggravate acidosis, should be used with caution.

In patients with a past history of renal calculi, benefit should be balanced against the risks of precipitating further calculi.

The pH of parenteral acetazolamide is 9.1. Care should be taken during intravenous administration of alkaline preparations to avoid extravasation and possible development of skin necrosis.

4.5 Interaction with other medicinal products and other forms of interaction
Acetazolamide is a sulphonamide derivative. Sulphonamides may potentiate the effects of folic acid antagonists. Possible potentiation of the effects of folic acid antagonists, hypoglycaemics and oral anti-coagulants.

Concurrent administration of acetazolamide and aspirin may result in severe acidosis and increase central nervous system toxicity. Adjustments of dose may be required when Diamox injection is given with cardiac glycosides or hypertensive agents. When given concomitantly Acetazolamide modifies the metabolism of phenytoin leading to increased serum levels of phenytoin. Severe osteomalacia has been noted in a few patients taking acetazolamide in combination with other anticonvulsants.

There have been isolated reports of reduced prindione and increased carbamazepine serum levels with concurrent administration of acetazolamide.

Because of possible additive effects with other carbonic anhydrase inhibitors, concomitant use is not advisable.

4.6 Pregnancy and lactation
Acetazolamide has been reported to be teratogenic and embryotoxic in rats, mice, hamsters and rabbits at oral or parenteral doses in excess of ten times those recommended in human beings. Although there is no evidence of these effects in human beings, there are no adequate and well-controlled studies in pregnant women. Therefore, Diamox injection should not be used in pregnancy, especially during the first trimester.

Acetazolamide has been detected in low levels in the milk of lactating women who have taken Diamox injection. Although it is unlikely that this will lead to any harmful effects in the infant, extreme caution should be exercised when Diamox injection is administered to lactating women.

4.7 Effects on ability to drive and use machines
Increasing the dose does not increase the diuresis and may increase the incidence of drowsiness and/or paraesthesia. Less commonly, fatigue, dizziness and ataxia have been reported. Diamox injection has been observed in a few patients with oedema due to hepatic cirrhosis. Such cases should be under close supervision. Transient myopia has been reported. These conditions invariably subside upon diminution or discontinuation of the medication.

4.8 Undesirable effects
Adverse reactions during short-term therapy are usually non-serious. Those effects which have been noted include: paraesthesia, particularly a “tingling” feeling in the extremities, some loss of appetite, taste disturbance, polyuria, flushing, thin hair, headache, dizziness, fatigue, depression, reduced libido and occasional instances of drowsiness and confusion. Rarely, photosensitivity has been reported.

During long-term therapy, metabolic acidosis and electrolyte imbalance may occasionally occur. This can usually be corrected by the administration of bicarbonate.

Transient myopia has been reported. This condition invariably subsides upon diminution or discontinuation of the medication.
Gastro-intestinal disturbances such as nausea, vomiting and diarrhoea. Acetazolamide is a sulphonamide derivative and therefore some side effects similar to those caused by sulphonamides have occasionally been reported. These include fever, agranulocytosis, thrombocytopenia, thrombocytic purpura, leucopenia and aplastic anaemia, bone marrow depression, pancytopenia, rash (including erythema multiforme, Stevens-Johnson Syndrome, toxic epidermal necrolysis), anaphylaxis, crystalluria, calculus formation, renal and ureteral colic and renal lesions. Rarely, fulminant hepatic necrosis has been reported.

Other occasional adverse reactions include: urticaria, melaena, haematuria, glycosuria, impaired hearing and tinnitus, abnormal liver function, renal failure and, rarely, hepatitis or cholestatic jaundice, flaccid paralysis and convulsions.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation 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 via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

4.9 Overdose
No specific antidote. Supportive measures with correction of electrolyte and fluid balance. Force fluids.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Carbonic anhydrase inhibitors.
ATC Code: S01EC01.
Acetazolamide is an inhibitor of carbonic anhydrase. By inhibiting the reaction catalysed by this enzyme in the renal tubules, acetazolamide increases the excretion of bicarbonate and of cations, chiefly sodium and potassium, and so promotes alkaline diuresis.

Continuous administration of acetazolamide is associated with metabolic acidosis and resultant loss of diuretic activity. Therefore the effectiveness of Diamox injection in diuresis diminishes with continuous use.

By inhibiting carbonic anhydrase in the eye acetazolamide decreases intraocular pressure and is therefore useful in the treatment of glaucoma.

5.2 Pharmacokinetic properties
Acetazolamide has been estimated to have a plasma half-life of about 4 hours. It is tightly bound to carbonic anhydrase and accumulates in tissues containing this enzyme, particularly red blood cells and the renal cortex. It is also bound to plasma proteins. It is excreted unchanged in the urine, renal clearance being enhanced in the alkaline urine.

5.3 Preclinical safety data
Nothing of note to the prescriber.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
None.

6.2 Incompatibilities
None.

6.3 Shelf life
60 months.

6.4 Special precautions for storage
Do not store above 25°C.

6.5 Nature and contents of container
Diamox Injection is a white powder, packed in a transparent glass vial with a grey rubber stopper, aluminium ring seal and blue plastic plug. Before use, it is made into a solution, using at least 5ml water for injection.

Each carton contains 1 vial.

6.6 Special precautions for disposal
Reconstitute each vial of Diamox injection with at least 5ml of water for injection prior to use. The reconstituted solution is clear and colourless and does not contain an antimicrobial preservative. Any unused solution can be stored in a refrigerator for up to 24 hours but any unused solution after this period must be discarded.

The direct intravenous route of administration is preferred. Intramuscular injection may be employed but is painful due to the alkaline pH of the solution.
Acetazolamide Injection should not be taken if you are pregnant, think you are pregnant or are planning to become pregnant. It may be taken when breast feeding but only on the advice of the doctor.

Driving and using machines: If Acetazolamide Injection makes you feel drowsy or confused you should not drive or operate machines. Acetazolamide Injection can occasionally cause short-sightedness; if this happens and you feel that you can no longer drive safely, you should stop driving and contact your doctor.

Important information about some of the ingredients of Acetazolamide Injection:
This medicine contains less than 1 mmol sodium (23mg) per dose, i.e. essentially "sodium-free".

3. HOW YOU ARE GIVEN ACETAZOLAMIDE INJECTION
Acetazolamide Injection is a white powder which will be dissolved in water to make a solution for injection either into one of your veins (intravenous) or into one of your muscles (intramuscular). The dose varies from person to person depending on their condition. Your doctor will decide on the most appropriate dose. Before starting and during treatment your doctor will monitor your blood to check that treatment with Acetazolamide Injection is suitable for you.

If you are given more Acetazolamide Injection than you should:
As the injection will be administered by a doctor, it is unlikely that you will be given more than is necessary.

If you have any further questions on the use of this product ask your doctor.

4. POSSIBLE SIDE EFFECTS
Like all medicines, Acetazolamide Injection can cause side effects, although not everybody gets them.

All medicines can cause allergic reactions although serious allergic reactions are very rare. Any sudden wheeziness, difficulty in breathing, swelling of the eyelids, face or lips, rash or itching (especially affecting your whole body) should be reported to a doctor immediately.

Extremely rarely, Acetazolamide Injection can affect the cells in your blood. This could mean that you are more likely to catch infections and that your blood may not clot properly. If you have a sore throat or fever or you notice bruises or tiny red or purple spots on your skin you should contact your doctor immediately. If your muscles feel weak or you have fits, you should see your doctor immediately.

Common side effects include:
- headache
- diarrhoea
- feeling or being sick, loss of appetite, thirst, or a metallic taste in the mouth
- dizziness, loss of full control of arms or legs
- looking flushed
- a need to pass urine more often than normal
- tiredness or irritability
- feeling over-excited
- a tingling or numbness in the fingers or toes, or coldness in the extremities

Other side effects include:
- depression
- drowsiness or confusion
- a loss of interest in sex
- ringing in the ears or difficulty in hearing
- temporary short-sightedness which subsides when the dosage is reduced or treatment is stopped.

Rare cases of skin rashes including an increased sensitivity to sunlight have been reported. If you experience any unusual skin rashes, inform your doctor.

Very rarely, Acetazolamide Injection can affect the liver and kidneys. If you experience pain in your lower back, pain or burning when you pass urine, have difficulty in passing urine, or you stop passing urine, have blood in your urine, pale stools, or if your skin or eyes look slightly yellow, you should contact your doctor. You should also contact your doctor if your stools are black or tarry, or if you notice blood in your stools.

If you are given Acetazolamide Injection for a long time it can occasionally affect the amount of potassium, or sodium in your blood. Your doctor will probably take blood tests to check that this does not happen. You might also experience bone thinning or the risk of kidney stones with long-term therapy. High or low blood sugar levels may occasionally occur.
If any of the side effects becomes serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

Reporting of side effects:
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

By reporting side effects you can help provide more information on the safety of this medicine.

5. HOW TO STORE ACETAZOLAMIDE INJECTION
Keep out of the sight and reach of children.

Do not store above 25°C.
Any unused solution can be stored in a refrigerator for up to 24 hours but any unused solution after this period must be discarded.

Do not use after the expiry date. This date is printed on your pack. The Expiry date refers to last day of that month.

For single use only.
If the powder becomes discoloured or show any other signs of deterioration, consult your pharmacist who will tell you what to do.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION
What Acetazolamide Injection Contains:
The active substance is acetazolamide.
Each vial contains 500mg acetazolamide (as acetazolamide sodium).

What Acetazolamide Injection looks like and contents of the pack:
Acetazolamide Injection is a white powder, packed in a transparent glass vial with a grey rubber stopper, aluminium ring seal and blue plastic plug. Before use, it is made into a solution, using at least 5ml water for injection.

Each carton contains 1 vial.

MANUFACTURER AND PRODUCT LICENCE HOLDER
Manufactured by Mercury Pharmaceuticals Ltd., Capital House, 85 King William Street, EC4N 7BL, London, UK.

BAG Health Care GmbH, Amttsrichsstrabe 1-5, D-35423 Lich, Germany.

Procured from within the EU by Product Licence holder:
Star Pharmaceuticals Ltd., 5 Sandridge Close, Harrow, Middlesex HA1 1XD.
Repackaged by Servipharm Ltd.

Leaflet revision and issue date (Ref) 17.11.16[P-4]
1. NAME OF THE MEDICINAL PRODUCT
Acetazolamide 500mg Powder for Solution for Injection.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each vial contains 500 mg acetazolamide (as acetazolamide sodium).
For full list of excipients see section 6.1.

3. PHARMACEUTICAL FORM
White powder for solution for injection.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
Acetazolamide is an enzyme inhibitor which acts specifically on carbonic anhydrase. It is indicated in the treatment of:

i) Glaucoma: Acetazolamide injection is useful in glaucoma (chronic simple (open angle) glaucoma, secondary glaucoma and peripetrically in acute angle closure glaucoma where delay of surgery is desired in order to lower intraocular pressure) because it acts on inflow, decreasing the amount of aqueous secretion.

ii) Abnormal retention of fluid: Congestive heart-failure, drug-induced oedema, episodic fever, and chronic renal failure.

iii) Epilepsy: In conjunction with other anticonvulsants best results with effects on several segments of the nephron are desirable in the treatment of myoclonic jerk patterns, etc.

iv) Dehydration of carbonic acid reaction in the kidney. The result is a renal effect is due to the effect on the reversible hydration of carbon dioxide and formation of bicarbonate. The change from other medication to Acetazolamide injection should be gradual. Elderly: Acetazolamide injection should only be used with particular caution in elderly patients or those with potential obstruction in the urinary tract or with diabetics rendering their electrolyte balance precarious or with liver dysfunction.

4.2 Posology and method of administration
Routes of Administration: Intravenous or intramuscular injection. The direct intravenous route is preferred as intramuscular use is limited by the alkaline pH of the solution.

i) Glaucoma (simple acute congestive and secondary):
Adults: 250-1000mg per 24 hours, usually in divided doses for amounts over 250mg daily.

ii) Abnormal retention of fluid: Congestive heart-failure, drug-induced oedema.
Adults: For diuresis, the starting dose is usually 250-375mg once daily in the morning. If, after an initial response, the patient fails to continue to lose oedema fluid, do not increase the dose but allow for kidney recovery by omitting a day. Best results are often obtained on a regime of 250-375mg daily for two days, rest a day, and repeat or merely giving Acetazolamide injection every other day. The use of Acetazolamide injection does not eliminate the need for other therapy, e.g. digitalis, bed rest and salt restriction in congestive heart failure and proper supplementary therapy with elements such as potassium in drug-induced oedema. For cases of fluid retention associated with pre-menstrual tension, a daily dose(simple) of 125-375mg is suggested.

iii) Epilepsy
Adults: 250-1000mg daily in divided doses.
Children: 8-30mg/kg in daily divided doses and not to exceed 750mg/day.
The change from other medication to Acetazolamide injection should be gradual. Elderly: Acetazolamide injection should only be used with particular caution in elderly patients or those with potential obstruction in the urinary tract or with diabetics rendering their electrolyte balance precarious or with liver dysfunction.

4.3 Contraindications
Acetazolamide injection is contra-indicated in situations in which sodium and/or potassium blood levels are depressed, in cases of marked kidney and liver dysfunction, suprarenal gland failure and hyper-chloremic acidosis. Acetazolamide injection should not be used in patients with hepatic cirrhosis as this may increase the risk of hepatic encephalopathy. Long-term administration of Acetazolamide injection is contra-indicated in patients with chronic non-congestive angle-closure glaucoma since it may permit organic closure of the angle to occur while the worsening glaucoma is masked by lower intraocular pressure.

Acetazolamide injection should not be used in patients hypersensitive to sulphonamides.

4.4 Special warnings and special precautions for use
Suicidal ideation and behaviour have been reported in patients treated with antiepileptic agents in several indications. A meta-analysis of randomized placebo-controlled trials of anti-epileptic drugs has also shown a small increased risk of suicidal ideation and behaviour. The mechanism of this risk is not known and the available data do not exclude the possibility of an increased risk for Acetazolamide injection. Therefore patients should be monitored for signs of suicidal ideation and behaviours and appropriate treatment should be considered. Patients (and caregivers of patients) should be advised to seek medical advice should signs of suicidal ideation or behaviour emerge.

Increasing the dose does not increase the diuresis and may increase the incidence of drowsiness and/or paraesthesia.

Increasing the dose often results in a decrease in diuresis. Under certain circumstances, however, very large doses have been given in conjunction with other diuretics in order to secure diuresis in complete refractory failure. When Acetazolamide injection is prescribed for long-term therapy, special precautions are advisable. The patient should be cautioned to report any unusual skin rash. Periodic blood cell counts and electrolyte levels are recommended. Fatalities have occurred, although rarely, due to severe reactions to sulphonamides. A precipitous drop in formed blood cell elements or the appearance of toxic skin manifestations should call for immediate cessation of Acetazolamide injection therapy.

In patients with pulmonary obstruction or emphysema where alveolar ventilation may be impaired, Acetazolamide injection which may aggravate acidosis, should be used with caution.

In patients with a past history of renal calculi, benefit should be balanced against the risks of precipitating further calculi.

The pH of parenteral acetazolamide is 9.1. Care should be taken during intravenous administration of alkaline preparations to avoid extravasation and possible development of skin necrosis.

4.5 Interaction with other medicinal products and other forms of interaction
Acetazolamide is a sulphonamide derivative. Sulphonamides may potentiate the effects of folic acid antagonists. Possible potentiation of the effects of folic acid antagonists, hypoglycaemics and oral anti-coagulants. Concurrent administration of acetazolamide and aspirin may result in severe acidosis and increase central nervous system toxicity. Adjustments of dose may be required when Acetazolamide injection is given with cardiac glycosides or hypertensive agents. When given concomitantly Acetazolamide modifies the metabolism of phenytoin leading to increased serum levels of phenytoin. Severe osteomalacia has been noted in a few patients taking acetazolamide in combination with other anticonvulsants. There have been isolated reports of reduced primidone and increased carbamazepine serum levels with concurrent administration of acetazolamide.

Because of possible additive effects with other carbonic anhydrase inhibitors, concomitant use is not advisable.

4.6 Pregnancy and lactation
Acetazolamide has been reported to be teratogenic and embryotoxic in rats, mice, hamsters and rabbits at oral or parenteral doses in excess of ten times those recommended in human beings. Although there is no evidence of these effects in human beings, there are no adequate and well-controlled studies in pregnant women. Therefore, Acetazolamide injection should not be used in pregnancy, especially during the first trimester.

Acetazolamide has been detected in low levels in the milk of lactating women who have taken Acetazolamide injection. Although it is unlikely that this will lead to any harmful effects in the infant, extreme caution should be exercised when Acetazolamide injection is administered to lactating women.

4.7 Effects on ability to drive and use machines
Increasing the dose does not increase the diuresis and may increase the incidence of drowsiness and/or paraesthesia. Less commonly, fatigue, dizziness and ataxia have been reported. Disorientation has been observed in a few patients with oedema due to hepatic cirrhosis. Such cases should be under close supervision. Transient myopia has been reported. These conditions invariably subside upon diminution or discontinuance of the medication.

4.8 Undesirable effects
Adverse reactions during short-term therapy are usually non-serious. Those effects which have been noted include: paraesthesia, particularly a "tingling" feeling in the extremities, some loss of appetite; taste disturbance, polyuria, flushing, thirst, headache, dizziness, fatigue, irritability, depression, reduced libido and occasional instances of drowsiness and confusion. Rarely, photosensitivity has been reported.

During long-term therapy, metabolic acidosis and electrolyte imbalance may occasionally occur. This can usually be corrected by the administration of bicarbonate.
Transient myopia has been reported. This condition invariably subsides upon diminution or discontinuation of the medication.

Gastro-intestinal disturbances such as nausea, vomiting and diarrhoea.

Acetazolamide is a sulphonamide derivative and therefore some side effects similar to those caused by sulphonamides have occasionally been reported. These include fever, agranulocytosis, thrombocytopenia, thrombocytic purpura, leucopenia and aplastic anaemia, bone marrow depression, pancytopenia, rash (including erythema multiforme, Stevens-Johnson Syndrome, toxic epidermal necrolysis), anaphylaxis, crystalluria, calculus formation, renal and ureteric colic and renal lesions. Rarely, fulminant hepatic necrosis has been reported.

Other occasional adverse reactions include: urticaria, melena, haematuria, glycosuria, impaired hearing and tinnitus, abnormal liver function, renal failure and, rarely, hepatitis or cholestatic jaundice, flaccid paralysis and convulsions.

**Reporting of suspected adverse reactions**
Reporting suspected adverse reactions after authorisation 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 via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

4.9 Overdose
No specific antidote. Supportive measures with correction of electrolyte and fluid balance. Force fluids.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Carbonic anhydrase inhibitors.
ATC Code: S01EC01.
Acetazolamide is an inhibitor of carbonic anhydrase. By inhibiting the reaction catalysed by this enzyme in the renal tubules, acetazolamide increases the excretion of bicarbonate and of cations, chiefly sodium and potassium, and so promotes alkaline diuresis.

Continuous administration of acetazolamide is associated with metabolic acidosis and resultant loss of diuretic activity. Therefore the effectiveness of Acetazolamide in diuresis diminishes with continuous use.

By inhibiting carbonic anhydrase in the eye acetazolamide decreases intraocular pressure and is therefore useful in the treatment of glaucoma.

5.2 Pharmacokinetic properties
Acetazolamide has been estimated to have a plasma half-life of about 4 hours. It is tightly bound to carbonic anhydrase and accumulates in tissues containing this enzyme, particularly red blood cells and the renal cortex. It is also bound to plasma proteins. It is excreted unchanged in the urine, renal clearance being enhanced in the alkaline urine.

5.3 Preclinical safety data
Nothing of note to the prescriber.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
None.

6.2 Incompatibilities
None.

6.3 Shelf life
60 months.

6.4 Special precautions for storage
Do not store above 25°C.

6.5 Nature and contents of container
Acetazolamide Injection is a white powder, packed in a transparent glass vial with a grey rubber stopper, aluminium ring seal and blue plastic plug. Before use, it is made into a solution, using at least 5ml water for injection.

Each carton contains 1 vial.

6.6 Special precautions for disposal
Reconstitute each vial of Acetazolamide injection with at least 5ml of water for injection prior to use. The reconstituted solution is clear and colourless and does not contain an antimicrobial preservative. Any unused solution can be stored in a refrigerator for up to 24 hours but any unused solution after this period must be discarded.

The direct intravenous route of administration is preferred. Intramuscular injection may be employed but is painful due to the alkaline pH of the solution.