PATIENT INFORMATION LEAFLET

Lepquity (valproic acid) can seriously harm an unborn child when taken during pregnancy. It can cause serious birth defects to body organs and/or body structures as well as harm the developing brain of the foetus and can also affect the way in which the child develops as it grows. Children whose mothers took Lepquity during pregnancy may have problems with early childhood development. Children affected can be slow to walk and talk, be intellectually less able than other children, and have difficulties with language and memory.

Children whose mothers took Lepquity during pregnancy have an increased risk of developing autistic spectrum disorders, childhood autism and attention deficit hyperactivity disorder (ADHD).

Your female (girl) child should not be given Lepquity if the Risk Minimisation Measures (Pregnancy Prevention Programme), have not been explained to her and yourself and if she cannot commit to follow the pregnancy risk minimisation measures.

SCHEDULING STATUS: **S3**

Lepquity, 250 mg/5 mL, syrup

Valproic acid

Contains methylparaben (0,12 % w/v) (preservative)

Contains propylene glycol 250 mg/5 mL (50 mg/mL)

Contains sodium hydroxide 69,5 mg per 5 mL

Contains sugar (sucrose 2,35 g/5 mL)

Contains sweetener (sorbitol)

Read all of this leaflet carefully before you start taking Lepquity

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.

- Lepquity has been prescribed for your child and you should not share their medicine with other people. It may harm them, even if their symptoms are the same as your child's.

What is in this leaflet

1. What Lepquity is and what it is used for

2. What you need to know before you give Lepquity

3. How to give Lepquity

4. Possible side effects

5. How to store Lepquity

6. Contents of the pack and other information

1. What Lepquity is and what it is used for

Lepquity contains a medicine called valproic acid. This belongs to a group of medicines called anti-convulsant or anti-epileptic medicines.

Lepquity is used to treat epilepsy (fits) in children.

2. What you need to know before you take Lepquity

Do not give Lepquity:

- if your child is hypersensitive (allergic) to valproic acid (active ingredient) or any of the other ingredients of Lepquity (listed in section 6).
- if your child has liver problems.
- if your child has a family history of liver problems.
- if your child suffers from porphyria (a rare metabolic condition).
- if your child has pancreatic problems.
- if your child has a genetic problem causing a mitochondrial disorder (e.g. Alpers-Huttenlocher syndrome)
- if your female (girl) child is pregnant, unless there is no suitable alternative treatment (see "Pregnancy and Breastfeeding: Pregnancy – Important advice for women").
- if your female (girl) child is able to have a baby, unless the conditions of the Pregnancy Prevention

Programme are met (see “Pregnancy and Breastfeeding: Pregnancy – Important advice for women”).

Your female child must not use Lepquity for preventing migraine when she is pregnant. Pregnancy should be excluded before starting treatment for migraine and your female child should use effect contraception.

If you think your child may have any of these problems, or if you are in any doubt at all, consult your doctor before giving Lepquity to your child.

Warnings and precautions

Take special care with Lepquity:

- if your child has bone marrow abnormalities
- if your child has a tendency to bruise or bleed easily
- if your child is younger than 3 years, or is mentally retarded
- if your child has kidney problems
- if your child has any mental disorders
- if your child has severe epileptic fits
- if your child experiences abdominal pain, nausea and/or vomiting: Contact your doctor immediately, as these may be symptoms of pancreatitis (inflammation of the pancreas). The risk of this potentially life-threatening condition is especially high in young children, in patients receiving combination treatment and in those with severe liver function disorder.
- Lepquity may cause marked and progressive weight gain. This is a very frequent side effect. Consult your doctor about appropriate strategies to minimise this risk.

Tell your doctor before starting Lepquity:

- if your child has lupus (an immune system condition affecting skin, bones and joints, lungs, kidneys).
- if your child is diabetic. Lepquity may give an indication that ketones are present in the urine when this is not the case.
- if your child has kidney problems. They may need a lower dose.
- if your child suffers from urea cycle enzymatic deficiency (a rare metabolic disorder)
- if you know that there is a genetic problem causing a mitochondrial disorder in your family.

Talk to your doctor even if your child no longer has these conditions but have had them in the past.

Your doctor may advise blood tests before you start giving Lepquity to your child and during the first six months of treatment.

A small number of people being treated with anti-epileptics such as Lepquity have had thoughts of harming or killing themselves. If at any time your child has these thoughts, immediately contact your doctor.

Other medicines and Lepquity

Always tell your healthcare provider if your child is taking any other medicine. (This includes all complementary or traditional medicines.)

Lepquity may potentiate the effect of:

- neuroleptic medicines (used to treat psychological disorders) – Lepquity may increase the effects of these medicines
- antidepressant therapy – medicines used to treat depression – including monoamine oxidase inhibitors and fluoxetine
- benzodiazepines, used as sleeping tablets or to treat anxiety
- other medicines used to treat epilepsy including phenobarbitone, phenytoin, primidone, lamotrigine, topiramate, carbamazepine and felbamate
- anticoagulants (used to prevent blood clots e.g warfarin)
- salicylates (aspirin) (see "Take special care with Lepquity: children below 3 years of age")
- zidovudine (used to treat HIV infections and AIDS)
- mefloquine and chloroquine (used to treat or prevent malaria) – may increase the likelihood of a fit. Before travelling to a malaria area, you should get advice from your doctor or pharmacist on the most appropriate prevention tablets.
- cimetidine (used to treat ulcers)
- cholestyramine (used to treat excessive high blood lipid (fat) levels)
- erythromycin (used to treat infections)
- carbapenem antibiotics such as imipenem, ertapenem and meropenem (antibiotics used to treat bacterial

infections). The combination of Lepquity and carbapenems should be avoided because it may decrease the effect of Lepquity

- temozolomide – used to treat cancer

Lepquity does not appear to influence the effect of oral contraceptives.

These medicines and others may be affected by Lepquity or affect how well it works. Your child may need different amounts of medicine, or your child may need to take different medicines. Your doctor will advise you.

Taking Lepquity with food and drink and alcohol

During treatment with Lepquity your child should not drink alcoholic beverages, as it may potentiate the effects of alcohol.

Pregnancy, breastfeeding and fertility

If your female child is pregnant or breastfeeding, or if you think your child may be pregnant or is planning to have a baby, please consult her doctor, pharmacist or other healthcare provider for advice before giving this medicine to your child.

Pregnancy

You should not give Lepquity to your child if she is pregnant or breastfeeding her baby (see "BEFORE YOU TAKE OR ARE GIVEN LEPQUITY").

Important advice for women:

If your female child is pregnant, she must not use Lepquity, unless her doctor has determined there is no suitable alternative treatment.

If your female child is able to have a baby, she must not use Lepquity unless the conditions of the Pregnancy Prevention Programme are met.

Lepquity can be harmful to unborn children when taken by female children during pregnancy. Lepquity can cause serious birth defects and can affect the way in which the child develops as it grows.

The conditions of the Pregnancy Prevention Programme require that before Lepquity is prescribed for your female child:

- your doctor must explain what might happen to the baby if she becomes pregnant while taking Lepquity. You need to ensure she understand these risks.
- your female child will be asked to perform a pregnancy test before starting Lepquity, or thereafter if needed. This is to make sure she is not pregnant.
- effective birth control (contraception) will be recommended for your female child (if appropriate) to avoid becoming pregnant while taking Lepquity.
- your doctor will assess your female child's understanding of contraception and the need for contraception without interruption during the entire duration of treatment with Lepquity.
- your doctor will review your female child's treatment regularly (at least once a year).
- your doctor will explain what to do if your female child decides later that she wants to have a baby. If your female child is planning to have a baby, she must first discuss this with her doctor. Your female child must not stop taking Lepquity or interrupt her method of contraception until she has discussed this with her doctor.
- parents or caregivers of a female child treated with Lepquity, must contact the doctor once the female child using Lepquity experiences her first menstrual period.

Please choose the situation which applies to your female child and read the descriptions that follow:

- MY FEMALE CHILD IS STARTING TREATMENT WITH LEPQUITY (First Prescription)
- MY FEMALE CHILD IS TAKING LEPQUITY AND IS NOT PLANNING TO HAVE A BABY
- MY FEMALE CHILD IS TAKING LEPQUITY AND IS PLANNING TO HAVE A BABY
- MY FEMALE CHILD IS PREGNANT AND IS TAKING LEPQUITY

MY FEMALE CHILD IS STARTING TREATMENT WITH LEPQUITY (First Prescription)

- If this is the first time your female child has been prescribed Lepquity, your doctor will have explained the risks to an unborn child if she becomes pregnant.
- If your female child is able to have a baby or once she is able to have a baby, she will need to make sure that she uses an effective method of birth control (contraception) throughout her treatment. Talk to her doctor or family planning clinic if she needs advice on contraception.
- Pregnancy must be excluded before start of treatment with Lepquity through the result of a pregnancy (blood) test, to be confirmed by her doctor.
- She must discuss appropriate methods of birth control (contraception) with her doctor.
- She must make sure she is using an effective method of birth control (contraception) during her entire treatment.
- She must get regular (at least annual) appointments with a medical practitioner experienced in the management of epilepsy.
- Tell her doctor at once if she is pregnant or you think she might be pregnant.
- Tell her doctor if she plans to become pregnant.
- It is important that you contact her doctor if your female child, treated with Lepquity, experiences her first menstrual period.

MY FEMALE CHILD IS TAKING LEPQUITY AND SHE IS NOT PLANNING TO HAVE A BABY

If she is continuing treatment with Lepquity and she does not plan to have a baby, make sure she is using an effective method of birth control (contraception), if applicable, without interruption during her entire treatment with Lepquity. Talk to her doctor or family planning clinic if she needs advice on contraception.

- Make sure she is using an effective method of contraception during her entire treatment.
- She must get regular (at least annual) appointments with a medical practitioner experienced in the management of epilepsy.
- Tell her doctor immediately if she pregnant or you think she might be pregnant.
- Tell her doctor if she plans to become pregnant.
- Parents or caregivers of a female child treated with Lepquity, must contact the doctor once the female child using Lepquity experiences her first menstrual period.

MY FEMALE CHILD IS TAKING LEPQUITY AND IS PLANNING TO HAVE A BABY

If she is on treatment with Lepquity and planning to have a baby, first schedule an appointment with her doctor. She should talk to her doctor long enough before she becomes pregnant so that she and her doctor can put several actions in place to ensure that her pregnancy goes as smoothly as possible, and any risks to her and her unborn child are reduced as much as possible. Her doctor may prescribe another medicine for her epilepsy which may have less risk for her baby.

She must not stop taking Lepquity or her birth control (contraception) until she has discussed this with her doctor. Her doctor will advise her on when she can stop her contraception.

Babies born to mothers who have been on Lepquity are at serious risk of birth defects and problems with development, which can be seriously debilitating.

Her doctor may want to adjust her treatment and/or prescribe dietary supplements of folic acid. Folic acid may lower the risk of spina bifida (a birth defect) and early miscarriage. However, it is unlikely that folic acid will reduce the risk of birth defects associated with Lepquity use.

She must not stop taking Lepquity unless her doctor agrees, as there are severe risks to herself and her developing baby if her epilepsy is not controlled.

If she is pregnant, or you think she might be pregnant, see her doctor immediately.

MY FEMALE CHILD IS PREGNANT AND IS TAKING LEPQUITY:

Women should not become pregnant while taking Lepquity. Your female child should use an effective method of birth control (contraception) and consult her doctor before planning pregnancy.

Lepquity has no effect on the efficacy of her oral contraceptive pill.

Schedule an urgent appointment with her doctor if she is pregnant or you think she might be pregnant. Her doctor will advise her further.

She should not stop taking Lepquity unless her doctor tells her to as her condition may become worse.

During pregnancy, should a mother suffer from a serious type of seizure, where the oxygen supply to her and her unborn baby may be cut off, the risk of death to the mother and unborn child is increased. Her doctor will advise her further.

Make sure your female child is referred to a medical practitioner experienced in the treatment of epilepsy to re-assess her treatment options.

She must get thorough counselling on the risks of Lepquity during pregnancy, including malformations and developmental effects in children.

Make sure she is referred to a medical practitioner for prenatal monitoring in order to detect possible occurrences of malformations.

The risks of Lepquity when taken during pregnancy:

- Babies born to mothers who are taking Lepquity, are at serious risk of birth defects and problems with development which can be seriously debilitating.
- It is known that in women who take Lepquity, around 10 babies in every 100 will have birth defects, as compared to 2 – 3 babies in every 100 born to women who do not have epilepsy.
- These birth defects to her developing baby include spina bifida (condition where bones of the spine are not properly developed), craniofacial defects (face and skull malformations), malformation of the limbs, heart, kidney and sexual organ malformations, hypospadias (malformation of the urethra) and multiple anomalies involving various body systems.
- Children born to mothers who take Lepquity during pregnancy, may have impaired physical and mental development or autistic disorders.
- It is estimated that up to 30 to 40 % of preschool children whose mothers took Lepquity during pregnancy may have problems with early childhood development. Children affected can be slow to walk and talk, less intellectually able than other children, and have difficulty with language and memory.
- It is therefore essential that she discusses her treatment with her doctor if she is thinking of becoming pregnant or tell her doctor as soon as she knows she is pregnant.
- Her doctor may want to adjust her treatment and/or prescribe dietary supplements of folate.

- She must not stop taking Lepquity unless her doctor agrees, as there are severe risks to herself and her developing baby if she has uncontrolled epilepsy.

Newborn babies of mothers who took Lepquity during pregnancy may have:

- blood clotting problems (blood not clotting very well). This may appear as bruising or bleeding which takes a long time to stop.
- hypoglycaemia (low blood sugar levels)
- hypothyroidism (underactive thyroid gland, which can cause tiredness or weight gain).
- withdrawal syndrome (agitation, irritability, hyper-excitability, jitteriness, hyperkinesia (muscle spasm), muscle problems, tremor, convulsions and feeding problems); when taken during the last trimester of pregnancy.

Breastfeeding

Lepquity passes into the breastmilk. She should not breastfeed her baby if she is taking Lepquity (See "BEFORE YOU TAKE OR ARE GIVEN LEPQUITY").

Fertility

Lepquity can cause infertility in both men and women.

Driving and using machines

In many cases the seizure control resulting from treatment with Lepquity may enable patients to actively drive.

However, take note of the risk that Lepquity may cause drowsiness or light-headedness especially in cases of combined therapy with several antiepileptics or concomitant treatment with benzodiazepines (anti-anxiety medicines).

It is not always possible to predict to what extent Lepquity may interfere with your child's daily activities. They should ensure that they do not engage in driving or operating machinery until they are aware of the

measure to which Lepquity affects them.

Lepquity contains propylene glycol (E 1520)

If your baby is less than 4 weeks old or your child is less than 5 years old talk to your doctor or pharmacist before giving them this medicine, in particular if the baby is given other medicines that contain propylene glycol or alcohol.

If your child suffers from a liver or kidney disease, they should not take Lepquity unless recommended by their doctor. Their doctor may carry out extra checks while they are taking Lepquity.

Lepquity contains sorbitol

This medicine contains 320 mg sorbitol in each 5 mL which is equivalent to 64 mg/mL.

Sorbitol is a source of fructose. If your doctor has told you that your child has an intolerance to some sugars or if they have been diagnosed with hereditary fructose intolerance (HFI), a rare genetic disorder in which a person cannot break down fructose, talk to their doctor before your child takes or receives this medicine.

Sorbitol may cause gastrointestinal discomfort and mild laxative effect.

Lepquity contains sodium

Lepquity contains 40 mg sodium (main component of cooking/table salt) in each 5 mL. This is equivalent to 2 % of the recommended maximum daily dietary intake of sodium for an adult.

Lepquity contains sugar (sucrose)

If your child has an intolerance to some sugars, contact their doctor before giving them Lepquity.

3. How to give Lepquity

Do not share medicines prescribed for your child with any other person.

Always give Lepquity exactly as their doctor or pharmacist has told you. You should check with your doctor, pharmacist or other healthcare professional if you are not sure.

For oral use only. Give this medicine by mouth.

Shake the bottle before use. Do not dilute Lepquity and it should be given in divided doses.

The usual dose is:

Children:

Children weighing less than 20 kg may be given 15 – 20 mg per kg per day.

Children weighing more than 20 kg may be given 450 mg daily in divided doses.

When treatment is first started, your child may be prescribed a lower dose. This is because some patients need less Lepquity than others to control their fits. Their doctor will increase the dosage until their condition is controlled. Because of this, it is very important that you follow the instructions their doctor has given you about how much to give. Blood tests may be needed.

Your doctor will tell you how long their treatment with Lepquity will last. Do not stop treatment early because they feel better. If you have the impression that the effect of Lepquity is too strong or too weak, tell your doctor or pharmacist.

If you give more Lepquity than you should

An overdose of Lepquity may be dangerous. Symptoms of acute overdose may include nausea, vomiting, dizziness, sometimes also serious, or even fatal, side-effects on the part of the central nervous system and breathing difficulty. In serious cases immediate medical assistance is required.

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.

The content of sodium in Lepquity may cause hypernatraemia (excessive sodium content in the body) when taken in excess.

If you forget to give Lepquity

If you forgot to give a dose at the right time, give it as soon as you remember. However, if it already nearing the time to give the next scheduled dose, do not give the forgotten dose and then continue treatment as prescribed.

Do not give a double dose to make up for forgotten individual doses.

If you stop giving Lepquity

Keep giving Lepquity until your child's doctor tells you to stop.

Do not stop giving your child Lepquity or alter the dose without checking with their doctor. If you stop giving your child, the medicine without their doctor's advice your child's condition may get worse.

4. Possible side effects

Lepquity can have side effects.

Not all side effects reported for Lepquity are included in this leaflet. Should your child's general health worsen or if they experience any untoward effects while receiving Lepquity, please consult their healthcare provider for advice.

If any of the following happens, stop giving Lepquity to your child and tell your doctor immediately or go to the casualty department at your nearest hospital:

- swelling of the hands, feet, ankles, face, lips and mouth or throat, which may cause difficulty in swallowing or breathing,
- rash or itching,
- fainting.

These are all very serious side effects. If your child has them, they may have had a serious reaction to Lepquity. They may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following in your child:

- bizarre behaviour associated with or not with more frequent or more severe fits, loss of drive, particularly

if phenobarbitone is taken at the same time or of Lepquity dose has been suddenly increased;

- repeated vomiting, extreme tiredness, abdominal pain, drowsiness, weakness, loss of appetite, nausea, jaundice (yellowing of the skin or white of the eyes), swelling of the legs or worsening of your epilepsy or a general feeling of being unwell;
- blood clotting problems;
- spontaneous bruising or bleeding;
- blisters and skin detachment.

These are all serious side effects. Your child may need urgent medical attention.

Tell your child's doctor if you notice any of the following in them:

Frequent

- nausea, diarrhoea and minor gastric irritation;
- temporary elevation of liver test values (which can be seen in blood tests) may occur at the beginning of treatment;
- nail and nail bed disorders.

Less frequent

- increased appetite leading to weight gain;
- disturbed coordination of movements and dizziness;
- confusion (occasionally followed by disturbed consciousness or associated with hallucinations or convulsions);
- oedema (swelling of the fingers, legs and toes);
- vasculitis (inflammation of the blood vessels);
- lethargy, temporary disturbance of brain functions, twitching of the eyes;
- impairment of hearing;
- reversible Fanconi's syndrome (a rare kidney disorder);
- skin rashes, e.g. rash;
- changes in women's periods;

- obesity;
- double vision;
- temporary loss of consciousness, Parkinson-like symptoms such as reduced capacity of movement, trembling (shakiness), increased muscular tension, involuntary movements, reversible dementia (impaired memory);
- excessive growth of facial or body hair;
- temporary hair loss;
- an increase in alertness, hyperactivity, aggression and inappropriate behaviour;
- bone disorders including osteopenia and osteoporosis (thinning of the bone) and fractures.

If any of these side effects continue, are severe or bother your child, tell your child's doctor, pharmacist or other healthcare professional.
If you notice any side effects in your child not mentioned in this leaflet, please inform your child's doctor or pharmacist.

Reporting of side effects

If your child gets side effects, talk to their doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on the SAHPRA website. By reporting side effects, you can help provide more information on the safety of Lepquity.

5. How to store Lepquity

Store all medicines out of reach of children.

Store at or below 30 °C.

Keep the container tightly closed

Do not use after the expiry date stated on the label / carton / bottle

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g., toilets).

6. Contents of the pack and other information

What Lepquity contains

- The active substance is valproic acid.
- The other ingredients are citric acid monohydrate, methylparaben, melon flavour 50997 C, propylene glycol (E 1520), sodium hydroxide, sorbitol (E 420) liquid, sucrose, purified water.

What Lepquity looks like and contents of the pack

Lepquity is a clear, colourless to light yellow solution with melon odour.

Lepquity syrup is packed in amber glass bottle 100 mL and covered by aluminium cap and placed into a folding box.

Holder of Certificate of Registration

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