Read all of this leaflet carefully before you start taking this medicine. If you have any further questions, ask your doctor or pharmacist.

1. WHAT ELDISINE IS AND WHAT IT IS USED FOR

Eldisine is a mixture of medicines. Cytotoxic medicines kill cells which are dividing, including cancer cells. It is used to treat patients who have a cancer such as leukaemia, malignant melanoma (a type of skin cancer) or breast cancer. If your doctor gives you this medicine for anything else, ask him or her if you have any questions.

2. HOW TO USE ELDISINE

You must inject Eldisine into a vein. Your doctor will only inject Eldisine into a vein.

3. HOW TO USE ELDISINE

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4. Possible side-effects

If you have any further questions, ask your doctor or pharmacist.

- Keep this leaflet. You may need to read it again.
- If you are taking other medicines, inform your doctor and pharmacist of these.

5. Contents of the pack and other information

1. WHAT IS ELDISINE AND WHAT IS IT USED FOR

Eldisine contains vincristine sulphate (Vindesine Sulphate) and is a cytotoxic medicine. Cytotoxic medicines kill cells which are dividing, including cancer cells. It is used to treat patients who have a cancer such as leukaemia, malignant melanoma (a type of skin cancer) or breast cancer. If your doctor gives you this medicine for anything else, ask him or her if you have any questions.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Eldisine Powder for Injection (Vindesine Sulphate) 5mg contains 5mg vindesine sulphate per 5ml when reconstituted.

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Eldisine Powder for Solution for Injection

A clear glass vial containing a lyophilised plug of white crystalline powder.

4. Clinical particulars

1. NAME OF THE MEDICINAL PRODUCT

Eldisine Powder for Solution for Injection 5.0 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Eldisine Powder for Solution for Injection 5.0 mg

3. PHARMACEUTICAL FORM

Eldisine Powder for Solution for Injection

A clear glass vial containing a lyophilised plug of white crystalline powder.

4. Clinical particulars

4.1 Therapeutic Indications

Eldisine is an anti-neoplastic drug for intravenous use which can be used alone or in combination with other antineoplastic drugs. Information available at present suggests that Eldisine as a single agent may be useful for the treatment of:

- acute lymphoblastic leukaemia
- childhood resistant to other drugs;
- blastic crises of chronic myeloid leukaemia;
- malignant melanoma unresponsive to other forms of therapy;
- advanced ovarian cancer unresponsive to appropriate endocrine surgery and/or hormonal therapy.

4.2 Pharmacology and mechanism of Action

This preparation is for intravenous use only. It should be administered only by individuals experienced in administration of vincristine.

5. HOW TO USE ELDISINE

Your doctor will only inject Eldisine into a vein. It must never be injected intrathecally (into your back with the needle going into your spine). If you have a bacterial infection, your doctor will probably treat the infections before starting the Eldisine.

Other medicines and Eldisine

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Pregnancy, breast-feeding and fertility

Hypersensitivity to vincristine sulphate or to any of the excipients listed in section 6.1

Special Warnings and Precautions for Use

1. Removal of as CSF is as safely possible through the lumbar access.

2. Insertion of an epidural catheter into the subarachnoid space via the intervertebral space above lumbar access and CSF irrigation with lactated Ringer's solution. Fresh frozen plasma should be requested and, when available, 25ml should be added to every 1 litre of lactated Ringer's solution.

3. Insertion of an intraventricular drain or catheter by a neurosurgeon and continuation of CSF drainage with lactated Ringer's solution and CSF irrigation daily or hourly. Based on the published management of survival cases involving the related vinca alkaloid vincristine sulphate, if vincristine is mistakenly given by the intrathecal route, the following treatment should be initiated immediately after the injection:

(a) After inadvertent intrathecal administration of vinca alkaloids, immediate neurological intervention is required in order to prevent devastating neurological sequelae, with limited recovery afterwards.

(b) After inadvertent intrathecal administration of vinca alkaloids, immediate neurological intervention is required in order to prevent devastating neurological sequelae, with limited recovery afterwards.

3. Insertion of an epidural catheter into the subarachnoid space via the intervertebral space above lumbar access and CSF irrigation with lactated Ringer's solution. Fresh frozen plasma should be requested and, when available, 25ml should be added to every 1 litre of lactated Ringer's solution.

(c) After inadvertent intrathecal administration of vinca alkaloids, immediate neurological intervention is required in order to prevent devastating neurological sequelae, with limited recovery afterwards.

CLINICAL PRACTICE

Intravenous use only – fatal if given by other routes

Intravenous use only – fatal if given by other routes

Extemporaneously prepared syringes containing this product must be packaged in an overwrap which is labelled “DO NOT REMOVE COVERING UNTIL MOMENT OF INJECTION. FOR INTRAVENOUS USE ONLY. INTRAVENOUS USE ONLY – FATAL IF GIVEN BY OTHER ROUTES.”

4.3 Contra-indications

FOR INTRAVENOUS USE ONLY – FATAL IF GIVEN BY OTHER ROUTES

See special warnings in section 4.4 for the treatment of patients given intravenous vincristine sulphate.

The intrathecal administration of vincristine sulphate usually results in death. Syringes containing this product should be labelled “FOR INTRAVENOUS USE ONLY – FATAL IF GIVEN BY OTHER ROUTES.”

5. HOW TO USE ELDISINE

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Other medicines and Eldisine

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4.5 Interaction with Other Medicinal Products and Other Forms of Interaction

When chemotherapy is being given in conjunction with radiotherapy through portals which include the liver, the use of vindesine is likely to be delayed until radiation therapy has been completed.

Acute shortness of breath and severe bronchospasm has been reported following the administration of vindesine. These reactions have been encountered most frequently when vindesine was used in combination with mitomycin-C and may be serious when there is pre-existing pulmonary dysfunction. The reaction may be instantaneous, or several hours after the drug is injected, and may occur up to 2 weeks after a dose of mitomycin-C. Progressive dyspnoea, requiring chronic therapy, may occur. Vindesine should not be re-administered.

The simultaneous oral or intravenous administration of phenytoin and antineoplastic chemotherapy combinations have been reported to have reduced blood levels of the anticonvulsant and increased seizure activity. Although the contribution of the vinca alkaloids has not been established, dosage adjustment of phenytoin may need to be made when used in combination with vindesine.

Cautions should be exercised in patients concurrently taking drugs shown to inhibit drug metabolism by P450 isoenzymes. For example, co-administration with furafylline, which is a competitive inhibitor of the CYP1A2 pathway may cause an earlier onset and/or an increased severity of side-effects. A vinca alkaloid may impair bone marrow function and cause neurotoxicity, dosage and side-effects should be carefully monitored when drugs with similar adverse effects are administered.

4.6 Fertility, Pregnancy and Lactation

Usage in pregnancy or lactation: The safety of this product for use during pregnancy has not been established. Animal studies with vindesine suggest that teratogenic effects may occur. The safety of this medicine during breast-feeding has not been established and mothers who are breast-feeding should be advised regarding contraception during treatment with vindesine due to the potential risks involved.

4.7 Effects on Ability to Drive and Use Machines

Not applicable.

4.8 Undesirable Effects

Prior to the use of the drug, patients and/or their parents/guardians should be advised of the possibility of antineoplastic side-effects. Antineoplastic toxicity appears to be related to the cumulative total dose given.

The following side-effects have been reported:

Gastro-intestinal: Nausea, vomiting, constipation, stomatitis, vesication of the mouth, ileus, diarrhoea, anorexia, abdominal pain, dysphagia, dyspepsia, perforated duodenal ulcer, nausea and vomiting usually may be controlled by anti-emetic agents).

Neuromuscular: Numbness and tingling of hands/feet (paresthesia), loss of the deep tendon reflexes, peripheral neuritis, mental depression, headache, convulsions, difficulties with balance, including dizziness and jaw pain.

Cutaneous: Alopecia from mild to total is the commonest side-effect. Regrowth of hair may occur while on therapy.

Miscellaneous: Cellulitis with extravasation. Injection site reaction (see section 4.2).

4.9 Overdose

Side effects following the use of vindesine are dose related. Therefore, following administration of more than the recommended dose, patients can be expected to experience these effects in an exaggerated fashion.

Supportive care should include: (a) daily blood counts for guidance in transfusion requirement; (b) monitoring of the syndrome of inappropriate secretion of antidiuretic hormone. This includes restriction of fluid intake and, perhaps, the use of a diuretic drug acting on the loop of Henle and distal tubule function; (c) use of cathartics to prevent ulcers; (d) administration of an anticonvulsant (e) monitoring the patient's cardiovascular system.

The use of folic acid in addition to the other supportive measures recommended may be considered, although, unlike vincristine, studies have not been conducted to confirm its protective action. Clinical experience of vindesine overdosage is extremely limited, with only one published case.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Pharmacodynamic properties: Vindesine sulphate is a vinca alkaloid and produces antineoplastic effects. It is metabolised primarily in the liver and excreted in the bile and faeces.

5.2 Pharmacokinetic Properties

The pharmacokinetics of vindesine are similar to those of the other vinca alkaloids. After intravenous administration, elimination from the blood is biphasic, the drug is rapidly distributed to body tissues. It is metabolised primarily in the liver and excreted in bile and urine.

5.3 Preclinical Safety Data

Animal studies with vindesine suggest that teratogenic effects may occur.

5.4 PHARMACOLOGICAL PROPERTIES

Eldisine is a white crystalline powder, supplied as a lyophilised plug in a rubber stoppered 10ml glass vial.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Eldisine contains

• The active substance in Eldisine is vindesine sulphate. Each 10ml bottle of Eldisine contains 5mg of vindesine sulphate.

• The other ingredient is mannitol (E421).

What Eldisine looks like and the contents of the pack

Eldisine is a white crystalline powder, supplied as a lyophilised plug in a rubber stoppered 10ml glass vial.

PL 09831/0117 Eldisine Powder for Solution for Injection 5 mg

Marketing Authorisation Holder and Manufacturer

Genus Pharmaceuticals Limited, Linwhistle, Huddersfield, HD7 8QH, UK.

Marketing Authorisation Holder: Genus Pharmaceuticals Limited.

This leaflet was last revised in August 2017

* Eldisine (vindesine sulphate) is a registered trademark of Genus Pharmaceuticals Limited.