

台灣大昌華嘉股份有限公司 函

地址：台北市內湖區堤頂大道2段407巷22號10樓
傳真：(02) 8752-6100
聯絡方式：(02) 2658-1000 分機：231
聯絡人：趙貞涵
E-MAIL：joanne.chao@dksh.com

受文者：天主教中華聖母修女會醫療財團法人

發文日期：民國 110 年 01 月 07 日

發文字號：嘉標字第 110-006 號

附件：原廠公文、許可證、新仿單。

主旨：本公司代理輝凌藥品股份有限公司之產品「Glypressin 0.1mg/ml Solution for Injection (可利新注射液 0.1 毫克/毫升)」仿單變更乙事，如說明段。

說明：

- 一、本公司代理輝凌藥品股份有限公司之「Terlipressin」成份相關產品「Glypressin 0.1mg/ml Solution for Injection 可利新注射液 0.1 毫克/毫升」，係用於出血性食道靜脈曲張，第一型肝腎症候群。
- 二、衛生福利部公告含 Terlipressin 藥品成分之中文仿單應於「不良反應」處刊載「上市後經驗：曾有通報引起橫紋肌溶解之案例」(發文字號：衛授食字第 1081410746 號)。此變更業已於 109 年 07 月 07 日通知在案 (嘉標字第 109-252 號)。
- 三、因應相關規定，自批號 S14975A 起產品即供應新版仿單。
- 四、特此通知，造成不便之處，敬祈見諒，並請繼續支持本公司為禱。

台灣大昌華嘉股份有限公司
負責人：伍安得



輝凌藥品股份有限公司 函

公司地址：台北市松江路 111 號 11 樓

傳 真：(02) 2515 8276

聯絡人及電話：杜宜憲 02-25158277 ext. 28

電子郵件信箱：ethan.tu@ferring.com

受文者：各醫療院所

發文日期：中華民國 109 年 12 月 29 日

發文字號：FT109122901 號

主 旨：變更敝公司治療出血性食道靜脈曲張，第一型肝腎症候群之「可利新注射液 0.1 毫克/毫升 Glypressin 0.1mg/mL Solution for Injection (衛署藥輸字第 025557 號)」仿單。

說 明：

一、「可利新注射液 0.1 毫克/毫升 Glypressin® 0.1mg/mL Solution」依據衛生福利部 108 年 10 月 29 日衛授食字第 1081410746 號函，根據上市後經驗加註不良反應，辦理仿單變更。

二、仿單比較表

部分	原始版本	變更版本
藥品不良反應	無。	上市後經驗：曾有通報引起橫紋肌溶解症之案例。

三、上述仿單變更自藥品批號 S14975A 包裝起始

敬請 鑒核

附件一、可利新注射液 0.1 毫克/毫升 Glypressin® 0.1mg/mL Solution 變更後仿單

藥商(公司)名稱：輝凌藥品股份有限公司

負 責 人：Didier Page

地 址：台北市中山區松江路 111 號 11 樓

電 話：02-25158277

聯絡人姓名：杜宜憲

印信戳記

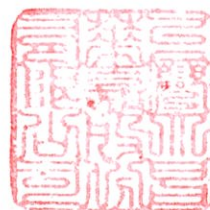
簽章

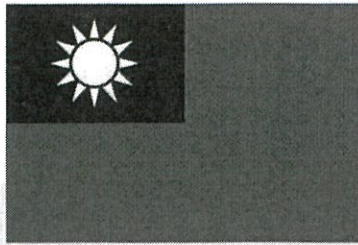


Didier Page

聯絡人電話：02-25158277#28

中 華 民 國 109 年 12 月 29 日





衛生福利部藥品許可證

衛署藥輸字第 025557 號

簽審文件號碼：DHA00202555701

中文名稱：可利新注射液 0.1 毫克/毫升

英文名稱：GLYPRESSIN 0.1mg/ml Solution for Injection

類別：限由醫師使用

藥商名稱：輝凌藥品股份有限公司

劑型：注射劑

製造廠名稱：ZENTIVA K.S.

包裝種類：8.5 毫升安瓿瓶裝，
5 安瓿盒裝

製造廠地址：U KABELOVNY 130, 102 37
PRAHA10, DOLNÍ MĚCHOLUPY,
CZECH REPUBLIC

處方：

Each ml contains:

Terlipressin free base 0.1MG (corresponding to 0.118MG Terlipressin acetate)

適應症：出血性食道靜脈曲張，第一型肝腎症候群。

前項藥品經本部審核與藥事法之規定相符應發給許可證以資證明

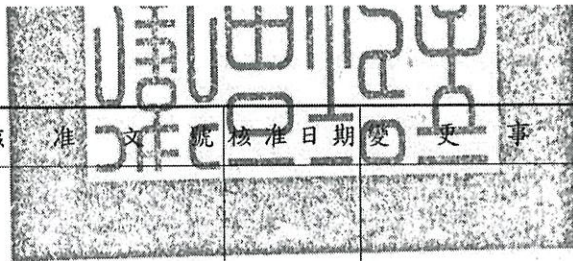
衛生福利部

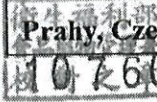
部長蔣丙煌

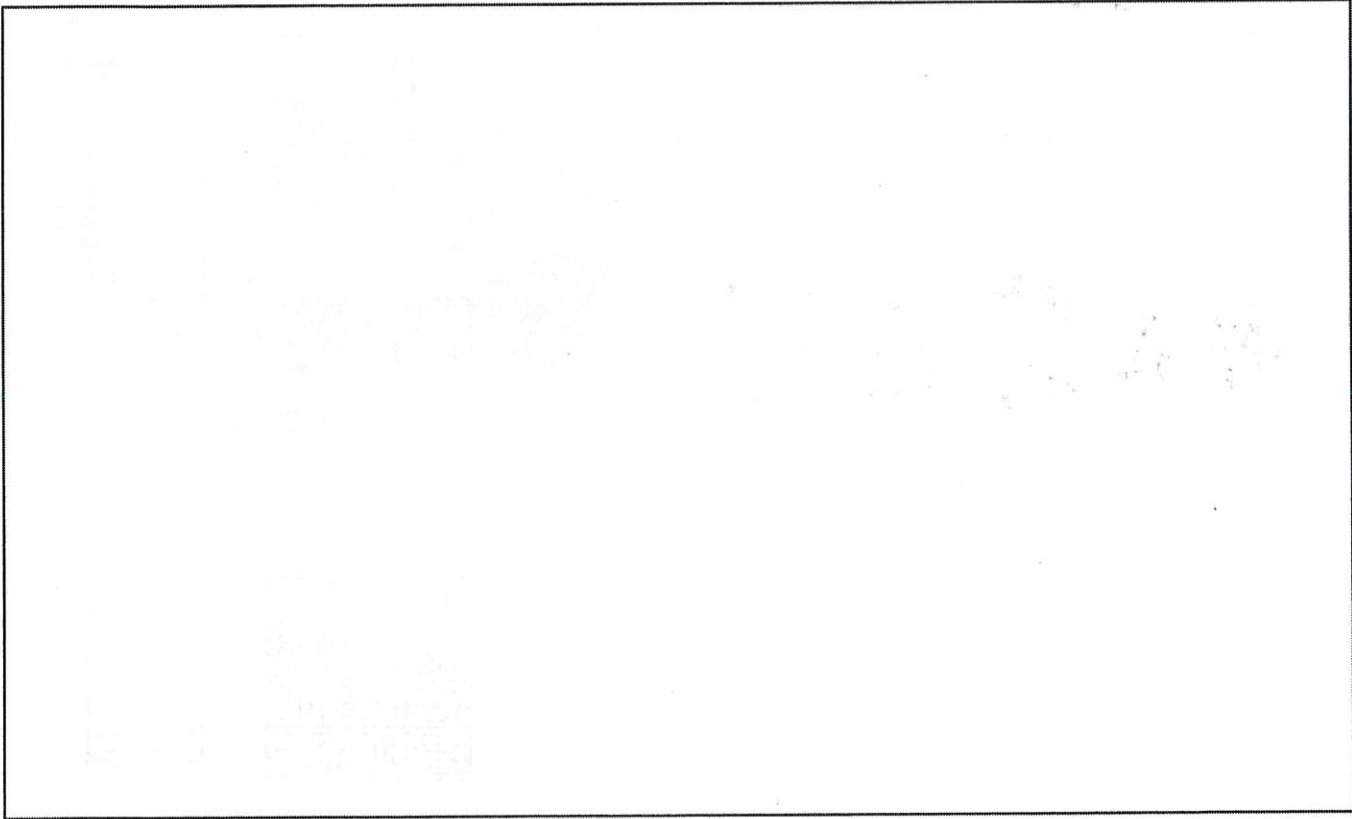
發證日期 105 年 2 月 22 日

有效日期 110 年 2 月 22 日

核准 展延 至	年 月 日	年 月 日	年 月 日	年 月 日
文號				



	變更事項核准			變更事項核准		
	變更事項	核准文號	核准日期	變更事項	核准文號	核准日期
其他	 108. 4. 29					
	新增三級包裝廠 Ferring-Léčiva, a.s Ke Skále 455, 252 42 Vestec u Prahy, Czech Republic  10. 7. 60 4 6 5 7 8					





EXT202008250007



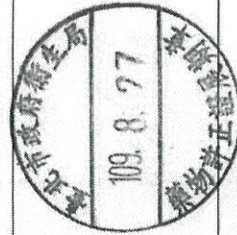
1091494258

☒ 藥品 ☐ 醫療器材 ☐ 輸入

☐ 含藥化粧品 ☐ 化粧品色素 ☐ 製造

許可證有效期間展延申請書

受文者	衛生福利部食品藥物管理署		申請日期	中華民國 109 年 08 月 25 日
主旨	☒ 「藥事法」 ☐ 依「化粧品衛生管理條例」之規定申請		文號	FT109082501
附件	附冊乙份共 1 頁	備註	■藥物許可證 ☐ 含藥化粧品、化粧品色素，有效期間之展延，請核辦。	
申請廠商	附件： 1. 藥品許可證。 2. 委託書。 3. 出產國許可製售證明。 4. 製造廠 PIC/S GMP 證明。 5. 有效成分之 GMP 證明及切結書。			
廠商名稱：輝凌藥品股份有限公司〈蓋章〉		Didier Page		
地址：台北市中山區松江路 111 號 11 樓		：Didier Page〈蓋章〉		
電話：02-25158277		監製者：林欣穎〈蓋章〉 管理		



衛生局加蓋章戳或註明事項

該藥商目前仍在營業中

林梅玉

0829/1115

☒藥品 ☐醫療器材 ☐輸入

☐含藥化粧品 ☐化粧品色素 ☐製造

許可證有效期間展延附冊

類別	品名(中、英文)	許可證字號 (備查文件字號)	有效期間			展延期間			審核結果
藥品	可利新注射液 0.1 毫克/毫升 GLYPRESSIN 0.1mg/ml Solution for Injection	衛署藥輸字第 025557 號	年	月	日	年	月	日	
			110	02	22	115	02	22	已

註：類別請填藥品、醫療器材或含藥化粧品、化粧品色素。

超過十件請另行檢附附冊。

GLYPRESSIN® 0.1 mg/ml Solution for Injection

COMPOSITION

One ampoule contains 1 mg terlipressin acetate.
One ampoule contains 135 mmol (or 30.7 mg) sodium.
For the full list of excipients, see section List of excipients.

PHARMACEUTICAL DOSAGE FORM

Solution for injection

Clear, colourless liquid

INDICATIONS

Bleeding oesophageal varices

Treatment of type 1 hepatorenal syndrome, characterised by spontaneous acute renal insufficiency, in patients suffering from severe cirrhosis, with ascites, as defined by the International Ascites Club criteria

DOSAGE AND ADMINISTRATION

Bleeding oesophageal varices

Adults

Initially an i.v. injection of 2 ampoules of GLYPRESSIN® solution for injection (2 mg terlipressin acetate, equivalent to 1.7 mg terlipressin) is given every 4 hours. The treatment should be maintained until bleeding has been controlled but up to a maximum of 48 hours. The dose can be adjusted to 1 ampoule of GLYPRESSIN® solution for injection (1 mg terlipressin acetate, equivalent to 0.85 mg terlipressin) i.v. every 4 hours in patients with body weight < 50 kg.

For maintenance dosage (if necessary), bolus injection of 1 ampoule of GLYPRESSIN® solution for injection every 4 hours for a maximum of 3 days.

Duration of treatment must not exceed 5 days.

In type 1 hepatorenal syndrome:

3 to 4 ampoules of GLYPRESSIN® solution for injection (3 to 4 mg terlipressin acetate, equivalent to 2.55 to 3.4 mg terlipressin) every 24 hours as 3 or 4 administrations.

In the absence of any reduction of the serum creatinine after 3 days of treatment, cessation of GLYPRESSIN® treatment is advised.

In the other cases, GLYPRESSIN® treatment is to be pursued until the obtaining either of a serum creatinine less than 130 µmol/litre or of a drop of at least 30 % in the serum creatinine with respect to the value measured at the time of diagnosis of hepatorenal syndrome.

The standard average duration of treatment is 10 days.

CONTRAINDICATIONS

Contraindicated in pregnancy

Hypersensitivity to terlipressin or to any of the excipients.

In patients with septic shock, with a low cardiac output terlipressin should not be used.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Blood pressure, heart rate and fluid balance should be monitored during treatment. Monitoring of diuresis and of the analysis of the electrolyte composition of the blood must be carried out in the case of treatment extending over several days. To avoid local necrosis at the injection site, the injection must be given i.v. Caution should be exercised in treating patients with hypertension or recognised heart disease like coronary insufficiency, renal dysfunction, cerebral or peripheral vascular disease, respiratory failure.

Children and the elderly: Particular caution should be exercised in the treatment of children and elderly patients, as experience is limited in these groups.

There is no data available regarding dosage recommendation in these special patient categories.

INTERACTION WITH OTHER MEDICAMENTS AND OTHER FORMS OF INTERACTIONS

The hypotensive effect of non-selective beta-blockers on the portal vein is increased with terlipressin. Concomitant treatment with medicinal products with a known bradycardic effect (e.g. propofol, sufentanil) may lower the heart rate and cardiac output. These effects are due to reflexogenic inhibition of cardiac activity via the vagus nerve due to the elevated blood pressure.

PREGNANCY AND LACTATION

Pregnancy

Treatment with GLYPRESSIN® during pregnancy is contraindicated (please refer to Contraindications and Preclinical safety data). GLYPRESSIN® has been shown to cause uterine contractions and increased intrauterine pressure in early pregnancy and may decrease uterine blood flow. GLYPRESSIN® may have harmful effects on pregnancy and foetus.

Spontaneous abortion and malformation has been shown in rabbits after treatment with GLYPRESSIN®.

Breastfeeding

It is not known whether terlipressin is excreted in human breast milk. GLYPRESSIN® should not be used in breast feeding women.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

No studies on the effects on the ability to drive and use machines have been performed.

UNDESIRABLE EFFECTS

The most commonly reported undesirable effects in clinical trials (frequency 1-10%) are: painless, increased blood pressure, abdominal pain, nausea, diarrhoea and headache.

The antidiuretic effect of GLYPRESSIN® may cause hyponatraemia unless the fluid balance is controlled.

Table: Frequency of undesirable effects

MedDRA System Organ Class	COMMON (≥1/100 to <1/10)	UNCOMMON (≥1/1000 to <1/100)	RARE (≥1/10000 to <1/1000)
Metabolism and nutrition disorders		Hyponaemia if fluid not monitored	
Nervous system disorders	Headache		
Cardiac disorders	Bradycardia	Atrial Fibrillation Ventricular Extrasystoles Tachycardia Chest pain Myocardial Infarction Fluid overload with pulmonary oedema Torsade de pointes Cardiac failure	
Vascular disorders	Peripheral vasoconstriction Peripheral ischaemia Facial pallor Hypertension	Intestinal ischaemia Peripheral cyanosis Hot flushes	
Respiratory, thoracic and mediastinal disorders		Respiratory distress Respiratory failure	Dyspnoea

Gastrointestinal disorders	Transient abdominal cramp Transient diarrhoea	Transient nausea Transient vomiting	
Skin and subcutaneous tissue disorders		Skin necrosis	
Pregnancy, puerperium and perinatal conditions		Uterine hypertonus Decreased uterine blood flow	
General disorders and administrative site conditions		Injection site necrosis	

Post-marketing experience: Cases of rhabdomyolysis have been reported.

OVERDOSAGE

The recommended dose (2 mg terlipressin acetate or 1.7 mg terlipressin / 4 hours) should not be exceeded as the risk of severe circulatory adverse effects is dose-dependent.

Elevated blood pressure in patients with recognised hypertension can be controlled with 150 mg clonidine i.v.

Bradycardia requiring treatment should be treated with atropine.

PHARMACODYNAMICS

Pharmacotherapeutic group: Posterior pituitary lobe hormones (vasopressin and analogues) ATC-code: H01BA04.

Terlipressin initially has an effect of its own, but is converted by enzymatic cleavage to lysine vasopressin. Doses of 1 and 2 mg terlipressin acetate effectively reduce the portal venous pressure and produce marked vasoconstriction. The lowering of portal pressure and azygos blood flow is dependent on dose. The effect of the low dose is reduced after 3 hours, while haemodynamic data show that 2 mg terlipressin acetate is more effective than 1 mg as the higher dose produces a dependable effect throughout the period of treatment (4 hours).

PHARMACOKINETICS

The pharmacokinetics follows a two-compartment model. It has been found that the half-life is approximately 40 min., metabolic clearance is approximately 9 ml/kg/min and the distribution volume is approximately 0.5 l/kg.

The desired concentration of lysine vasopressin in plasma is found initially after approximately 30 min. and reaches a peak value of 60 to 120 min. after administration of GLYPRESSIN®. Because of 100% cross-reaction between terlipressin and lysine vasopressin, there is no specific RIA method for these substances.

PRECLINICAL SAFETY DATA

Preclinical data reveal no special hazard for humans based on conventional studies of single- and repeat-dose toxicity, and genotoxicity. At dosages relevant to humans, the only effects observed in animals were those attributable to the pharmacological activity of terlipressin. No pharmacokinetic data are available from animals to compare with humans the plasma concentrations at which these effects occurred, but as the route of administration was intravenous, a substantial systemic exposure can be assumed for the animal studies.

An embryo-fetal study in rats demonstrated no adverse effects of terlipressin, but in rabbits abortions occurred, probably related to maternal toxicity, and there were ossification anomalies in a small number of fetuses and a single isolated case of cleft palate.

No carcinogenicity studies have been performed with terlipressin.

LIST OF EXCIPIENTS

Sodium chloride, acetic acid, sodium acetate trihydrate, water for injections

INCOMPATIBILITIES

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

SHELF-LIFE

2 years

STORAGE

Store in a refrigerator (2°C - 8°C). The ampoules are stored in the outer carton in order to protect from light.

PACKING SIZES

8.5 ml solution in clear colourless glass ampoules (Type I glass)

Box of 5 ampoules x 8.5 ml

SPECIAL PRECAUTIONS FOR DISPOSAL

Any unused drug or waste materials should be disposed of in accordance with local requirements.

Manufacturer:

ZENTIVA s.r.o.,
U Kabelovny 130, 102 37 Praha 10
Dolní Měcholupy, Czech Republic

Packager:

ZENTIVA s.r.o.,
U Kabelovny 130, 102 37 Praha 10
Dolní Měcholupy, Czech Republic
or
Fering-Léčiva, a.s.
Ke Stále 435, 252 42 Vestec u Prahy, Czech Republic