REGIONE CAMPANIA
AZIENDA OSPEDALIERA DI CASERTA
SANT'ANNA E SAN SEBASTIANO
DI RILIEVO NAZIONALE E DI ALTA SPECIALIZZAZIONE

Determina Dirigenziale N. 28 del 25/01/2019

PROPONENTE: **UOC PROVVEDITORATO ED ECONOMATO**

OGGETTO: **Procedura negoziata, ai sensi dell'art.36 D.Lgs. n.50/2016, per l'affidamento della fornitura di n.480 fiale di Edavarone – CIG Z8C26C6D8D**

Il presente atto, in formato digitale e firmato elettronicamente, costituisce informazione primaria ed originale ai sensi dei combinati disposti degli artt. 23-ter, 24 e 40 del D.Lgs. n. 82/2005. Eventuale riproduzione analogica, costituisce valore di copia semplice a scopo illustrativo.

REGIONE CAMPANIA

AZIENDA OSPEDALIERA DI CASERTA

SANT'ANNA E SAN SEBASTIANO

DI RILIEVO NAZIONALE E DI ALTA SPECIALIZZAZIONE

Oggetto: Procedura negoziata, ai sensi dell'art.36 D.Lgs. n.50/2016, per l'affidamento della fornitura di n.480 fiale di Edavarone – CIG Z8C26C6D8D

Direttore UOC PROVVEDITORATO ED ECONOMATO

Premesso che

- il Direttore dell'U.O.C. Farmacia, con pec del 19.12.2018, ha richiesto l'acquisto di n.480 fiale di Edavarone 30 mg (all.1);

- come dichiarato dal Direttore UOC Farmacia, trattasi di farmaco estero, non presente su piattaforma SORESA e le ditte disponibili alla fornitura sono: Ottopharma srl, Farmaceutica Internazionale Italiana srl, Interfarmaci e Unipharma S.A. (all.1);

- al fine di provvedere in merito, con pec del 08.01.2018, sono state richieste offerte alle ditte Ottopharma srl, Farmaceutica Internazionale Italiana srl, Interfarmaci e Unipharma S.A.;

- entro il termine di scadenza fissato sono pervenute solo 2 offerte da parte delle ditte Unipharma S.A. e Ottopharma srl (all.2);

- le predette offerte sono state trasmesse al Direttore UOC Farmacia per relazione in merito alla conformità;

- l'offerta conforme al prezzo più basso è risultata quella presentata dalla ditta Unipharma S.A. per una spesa complessiva,comprensiva di spese di trasporto, pari ad € 2.766,00 + iva al 10% (alleg.3);

Considerato che

- la presente proposta di determinazione è formulata previa istruttoria ed estensione conformi alla normativa legislativa vigente in materia e può essere pubblicata integralmente;

DETERMINA

per i motivi espressi in narrativa di:

1. procedere all'acquisto presso la ditta Unipharma di n.480 fiale di Edavrone 30 mg per una spesa complessiva, comprensiva di spese di trasporto, pari ad € 3.042,60 iva al 10% inclusa;
2. imputare la spesa complessiva pari ad € 3.042,60 iva inclusa al 10%, sul conto economico n.501010101 all'autorizzazione di spesa di competenza del bilancio dell'anno 2019;

3. prevedere la clausola di recesso, ai sensi del combinato disposto dagli artt.92 e 100 del D.Lgs. 159/2011, qualora vengano accertati elementi relativi a tentativi di infiltrazione mafiosa;
4. prevedere la clausola risolutiva espressa in caso di successivi analoghi affidamenti centralizzati regionali da parte di SoReSa spa;
5. trasmettere copia della presente determinazione al Collegio Sindacale, come per legge, alle U.U.O.O.C.C GEF e Farmacia;

IL DIRETTORE UOC PROVVEDITORATO
ED ECONOMATO
DR.SSA MARISA DI SANO

Azienda Ospedaliera
di Caserta
Sant'Anna
e San Sebastiano
di rilievo nazionale
e di alta specializzazione

ALLEGATO N. 1

U.O.C. Farmacia

Caserta, 19/12/2018

Al Direttore U. O. C.
Provveditorato ed Economato

OGGETTO: Acquisto Farmaco Estero EDAVARONE

Con riferimento alla richiesta del Direttore dell'U.O.C. di Neurologia, che si allega, si chiede di predisporre gli atti amministrativi per consentire a questa U.O.C. l'acquisto del farmaco estero EDAVARONE 30mg fiale, non esclusivo, non presente in piattaforma So.Re.Sa.
Le ditte, a nostra conoscenza, disponibili alla fornitura del farmaco in oggetto sono Ottopharma srl, Farmaceutica Internazionale Italiana srl, Inter Farmaci Italia srl e Unipharma S.A.

Si precisa che il fabbisogno è quello presunto fino al 31/12/2019.

Cordiali saluti.

Dott.ssa Evelina Murtas
Responsabile AFE

Direttore U.O.C. di Farmacia
Dott.ssa Anna Dello Stritto

"31/10/2018 09.19-20180028619"

AZIENDA OSPEDALIERA S.ANNA E S.SEBASTIANO DI CASERTA
via Palasciano 81100 Caserta – Centralino 0823 231111
U.O.C. Neurologia
Direttore f.f. Dr. Roberto Rosato

Prot. N.

Caserta, lì 30/10/2018

Alla Cortese Attenzione della Dottoressa Anna Dello Stritto, Farmacia Ospedaliera AORN CE.

Oggetto: richiesta acquisto farmaco estero Edavarone

Gentile Dottoressa,

essendo codesta azienda considerata "Presidio di riferimento per Malattia rara --Sclerosi Laterale Amiotrofica- ai sensi del DGRC n.1362/2005", vista la richiesta dei pazienti affetti da tale malattia, si richiede l'acquisto di farmaco estero EDAVARONE commercializzato in fl da 30 mg.

Il fabbisogno presunto di tale farmaco, per 2 pazienti, per 12 mesi compreso il primo ciclo di somministrazione, è di 480 fiale.

Cordiali saluti.

Dott. Roberto Rosato

"SANT[illegible]NO"

Si conferma la richiesta in essere

Scanned with CamScanner

Unipharma SA
Via Figino, 6
6917 – Barbengo Lugano – Switzerland
Tel. +41 91 985 62 11
Fax. +41 91 985 62 22
E-mail: sales@unipharma.ch

Cert. N°23997

ALLEGATO N. 2

Offerta cliente

M-COM 05

DESTINATARIO	6137	**OFFERTA N°**	2019-19000088
Azienda:	Ospedale San Sebastiano	**Città:**	Caserta
Persona di riferimento:	Marisa DI SANO	**Reparto:**	UOC Provveditorato ed Economato
Fax:	provveditorato@ospedale.caserta.it	**Telefono:**	

MITTENTE

Autore messaggio:	WESSEL Federico	**Telefono:**	0041 91 985 62 11

Cambio mese corrente EUR 0.9 (pari a CHF 1.00) **Lugano,** 09.01.2019

Oggetto: Offerta - Edaravone

Egregi signori,
con riferimento alla vostra richiesta in oggetto abbiamo il piacere di allegare: listino prezzi, costi di spedizione e condizioni di vendita.

Per ulteriori informazioni potete contattare i numeri seguenti:

Ufficio vendite e pronta disponibilità
Direttore: Maurizio Nanni
Collaboratori: Monica Colombo, Mariangela Li Greci, Federico Wessel

Orari d'ufficio da lunedì a venerdì 08^{00}–12^{00}/13^{00}–17^{30}
E-mail: sales@unipharma.ch
Reperibilità nelle 24 ore al di fuori dell'orario d'ufficio telefonando semplicemente al numero abituale: 0041 91 985 62 11
Disponiamo del sito www.unipharma.ch al quale potete accedere per cercare i prodotti di cui necessitate.

Centro di documentazione scientifica e servizio informazione sui farmaci svizzeri ed esteri
Direttore tecnico: Francesco Natale Agustoni, *farmacista*

Banche dati: Compendium, Rote Liste, Vidal, Pharmavista, Tropimed, Phyto, Martindale, Medical letter, Internet e vasta documentazione tratta da riviste, pubblicazioni, biblioteche, ecc.

Ufficio di Sanità Aeroportuale	Ciampino	Tel/Fax 06 7949 4220
Corriere TNT		Numero verde 199 803 868

Ci auguriamo che la nostra offerta sia di vostro interesse e, assicurandovi fin da ora un servizio rapido ed accurato, distintamente vi salutiamo.

UNIPHARMA SA

WESSEL Federico

ALLEGATO N.2

OTTOPHARMA S.R.L.

VIA NOVARA, 38
28021 BORGOMANERO (NO)
C.F. – P.IVA IT 02457060032

OttoPharma

PROPOSTA DI FORNITURA

Spett.le
ASL CASERTA
VIA UNITA' ITALIANA 28
81100 CASERTA CE

N°	Data	Pagina	Cliente
90059	**08/01/19**	**1**	**26**

Spedizione	Porto
A MEZZO CORRIERE	**FRANCO**

Cod. Pag.	Modalità Pagamento	Consegna
1	**60 GG BONIFICO D.F.**	

Codice Articolo	Descrizione Articolo	UM	Quantità	Prezzo Unitario	Importo Totale
FAR1396	CRITIVON 1,5MG/ML 1 F.LA 20ML	CF	1	12,40	12,40
	(EDARAVONE)				
	SPESE TRASPORTO			15,00	15,00
	PRODUTTORE:PACE BIOTECH				
	PROVENIENZA:INDIA				
	CONSEGNA: 10-12 GG LAVORATIVI				
	Tutti i prezzi sono da				
	intendersi I.V.A. 10% esclusa				
	Spese di importazione:				
	GRATUITE				
	>> LA PRESENTE OFFERTA SI				
	INTENDE VALIDA FINO AL				
	31/12/2019 <<				
	**Salvo aumenti disposti dalla				
	Ditta produttrice				

GLI ORDINI ANDRANNO INOLTRATI A: E-MAIL: ordini@ottopharma.com in alternativa FAX: 0322-060732

Le informazioni contenute nella presente comunicazione sono di natura privata e come tali riservate ed inviate esclusivamente al destinatario indicato in epigrafe. La diffusione, la distribuzione e/o la riproduzione non espressamente autorizzata di quanto trasmesso, da parte di qualsiasi soggetto diverso dal suo destinatario, è proibita ai sensi del D.lgs 196/03. Qualora per errore vi sia stato trasmesso il seguente documento vorrete cortesemente darcene immediata comunicazione inviando un messaggio alla e-mail del mittente.

Prescription Drug

EDARAVONE

Injection 30mg

- Free radical scavenger -

Composition:
Each ml contains:
Edaravone 1.5 mg
Water for injection I.P. q.s

Dose Form : Clear aqueous solution for injection.

Description :Edaravone is a neuroprotective agent used for the purpose of aiding neurological recovery following acute brain ischemia (inadequate blood supply), subsequent cerebral infarction . It acts as an potent antioxidant and strongly scavenges free radicals protecting against oxidative stress occurred apoptosis .

PHARMACOLOGY

1. **Mechanism of action**

1. Free radicals such as hydroxyl radical (·OH) play a major causative role in the development of cerebral vascular disorder resulting from ischaemia. During ischaemia or ischaemic reperfusion,there is increase the production of free radicals. These free radicals peroxidize unsaturated fatty acid of cell membrane lipids, which leads to cell membrane injury and ultimately to cerebral dysfunction. Although the **etiology** of development and disease progress of amyotrophic lateral sclerosis (ALS) are unknown, a possible involvement of oxidative stress caused by free radicals is suggested.
2. Edaravonescavenges free radicals and inhibits lipid peroxidation, and thereby prevents oxidative damage to brain cells (vascular endothelial cells/nerve cells).

In other words, Edaravonepromotes the brain in case of acute ischaemic stroke by exerting its inhibitory effects against the development and progression (exacerbation) of ischaemic cerebral vascular disorder such as cerebral oedema, cerebral infarction, neurological deficits, and delayed neuronal death. In case of amyotrophic lateral sclerosis (ALS), Edaravone suppresses the disease progression by exerting its inhibitory effects against the development of oxidative damage to nerve cells.

2. **Effects against the acute ischaemic stroke**

(1) **Neuroprotective effect**[2]

NAA (N-acetyl aspartate) is a specific marker for viable neuronal cells that is reported to decrease immediately after the onset of ischaemic stroke and be scarcely detected in the injured tissues after 24 hours. When NAA was determined by ^{1}H-MRS (magnetic resonance spectroscopy) after ad-ministration of Edaravone to patients with acute ischaemic stroke, NAA in the center of the infarct lesion was significantly retained on the 28th day after onset as compared to the control group.

(2) **Inhibitory effect against a reduction in regional blood flow in the ischaemic penumbre**[3]

When regional cerebral blood flow was determined by ^{133}Xe-SPECT (single photon emission computerized to-mography) after administration of Edaravoneto patients (n=8) with acute ischaemic stroke, Edaravone exhibited its inhibitory effect against the reduction in regional cerebral blood flow in the ischaemic penumbra in 5 patients who improved in functional outcomes (modified Rankin Scale).

3. **Cerebroprotecting effect in a cerebral ischaemia model**

Edaravone : Effects of inhibiting cerebral oedema and ischaemic stroke and of alleviating neuroiogical deficits
Edaravone :Inhibitory effect against delayed neuronal death .

4. **Free radical scavenging effect**

(1) **Edaravone exihibit Free radical scavenging effect and inhibitory effect against lipid peroxidation** (*in vitro*)

(2) **Edaravone exihibit also Free radical scavenging effect in a cerebral ischaemia model**

(3) **Inhibitory effect against vascular endothelial cell injury caused by free radical** (*in vitro*)

5. **Non-clinical studies related to disease conditions of amyotrophic lateral sclerosis (ALS) but when edaravone was administered its shows significant inhibitory effect.**

PHARMACOKINETICS

1. **Plasma concentration**

The profiles of plasma unchanged drug concentrations after multiple intravenous doses (0.5 mg/kg) over 30 minutes twice a day for 2 days to 5 healthy male adults and 5 healthy elderly males aged 65 years (Note). The approved dose of Edaravone is 30 mg per one time for use in patients with acute ischaemic stroke and 60 mg per one time for use in patients with amyotrophic lateral sclerosis (ALS). The plasma unchanged drug concentration disappeared in both healthy adults and elderly males in the almost same way without any signs of accumulation.

2. **Serum protein binding rates**

The binding rates of edaravone (5μM and 10μM) in human serum protein and human serum albumin were 92% and 89.91%, respectively (*in vitro*).

3. **Metabolism** The major metabolite in healthy male adults and healthy elderly males was sulfate conjugate in plasma, and glucuronide conjugate was also detected in plasma. In urine, the major metabolite of the product was glucuronide conjugate and sulfate conjugate was also detected.

4. **Excretion**

After repeated intravenous administration of Edaravone to healthy male adults and healthy elderly males twice a day for 2 days (0.5 mg/kg/30 minutes X 2 times/day), 0.7-0.9% and 71.0-79.9% of the dose were recovered as unchanged drug and metabolites in urine, respectively, up to 12 hours after each dose.

(Note) The approved dose of Edaravone is 30 mg per one time for use in patients with acute ischaemic stroke and 60 mg per one time for use in patients with amyotrophic lateral sclerosis (ALS).

INDICATIONS:

1. Improvement of neurological symptoms, disorder of activities of daily living, and functional disorder associated with acute ischaemic stroke
2. Inhibition on progression of functional disorder in patients with amyotrophic lateral sclerosis (ALS)

DOSING:

The approved dose of Edaravone is 30 mg per one time for use in patients with acute ischaemic stroke and 60 mg per one time for use in patients with amyotrophic lateral sclerosis (ALS)

DOSAGE AND ADMINISTRATION

The usual adult dosage is one ampoule (30 mg of edaravone) diluted with an appropriate volume of physiological saline, etc., which is administered intravenously over 30 minutes twice a day in the morning and the evening.
Administration should be initiated within 24 hours after the onset of the disease, and the duration of ad-ministration should be within 14 days.

The usual adult dosage is two ampoules (60 mg of edaravone) diluted with an appropriate volume of physiological saline, etc. which is administered intravenously over 60 minutes once a day.
Usually, the duration of administration and cessation are combined as one cycle of treatment for 28 days and the cycle should be repeated. Edaravone is consecutively infused for 14 days in the duration of administration followed by cessation for 14 days in the 1st cycle, and from the 2nd cycle, is infused for 10 of 14 days in the duration of administration followed by cessation for 14 days

Adverse Reactions

(1) **Clinically significant adverse reactions**

1) **Acute renal failure** (0.26%), **nephrotic syndrome** (0.02%): Renal function tests should be performed frequently and patients should be monitored carefully, since acute renal failure or nephrotic syndrome may occur. discontinued the use of Edaravone and appropriate therapeu-tic measures should be taken, when decreased renal func-tion and/or the symptoms of oliguria, etc. are found.

2) **Fulminant hepatitis** (incidence unknown), **hepatic dysfunction** (0.24%), **jaundice** (incidence unknown): Liver function tests should be performed frequently, and patients should be monitored carefully, since severe hep-atitis including fulminant hepatitis, hepatic dysfunction or jaundice with significant increase in AST (GOT), ALT (GPT), Al-Py GTP, LDH, blood bilirubin, etc. may oc-cur. Edaravone should be discontinued and appropriate therapeutic measures should be taken when any abnor-malities are found.

3) **Thrombocytopenia** (0.08%), **granulocytopenia** (inci-dence unknown): Hematological tests should be per-formed frequently and patients should be monitored carefully, since thrombocytopenia or granulocytopenia may occur. Edaravone should be discontinued and ap-propriate therapeutic measures should be taken, when any abnormalities are found.

4) **Disseminated intravascular coagulation (DIC)** (0.08%): Hematological tests should be performed peri-odically, since DIC may occur. Edaravone should be discontinued and appropriate therapeutic measures should be taken, when any abnormalities in hematological tests or symptoms suspicious of DIC are found.

5) **Acute lung injury** (incidence unknown): Patients should be monitored carefully, since acute lung injury with py-rexia, cough, dyspnoea and chest X-ray abnormalities may occur. Edaravone should be discontinued and appro-priate therapeutic measures, including administration of corticosteroids, should be taken, when any signs of acute lung injury are found.

6) **Rhabdomyolysis** (incidence unknown): Patients should be monitored carefully, since rhabdomyolysis may occur. Edaravone should be discontinued and appropriate therapeutic measures should be taken, when myalgia, weakness, increased CK (CPK) and increased blood and/or urine myoglobin are found.

7) **Shock, anaphylactoid reaction** (incidence unknown, each): Patients should be monitored carefully, since shock and anaphylactoid reactions (urticaria, blood pressure decreased and dyspnoea, etc.) may occur. Edaravone should be discontinued and appropriate therapeutic measures should be taken, when any abnormalities are found.

Use in the Elderly : When there is any adverse effect of Edaravone discontinued its use . Special caution should be exercised ,since many fatal cases have been reported in these patients.

Use during Pregnancy , Delivery or lactation

(i)Edaravone is not recommended to be administrated to pregnant women or women who may possible be pregnant .

(ii) Lactation should be prohibited during administration Edaravone .

Pediatric Use : Edaravone in children has not been established

Precaution & Warning:

1.Carefully administration : Edaravone should be administered with care to these Patients who suffers with renal impairment or dehydration ,infections , hepatic impairment ,cardiac diseases, & severe disturbance of consciousness.

2.Important points

(1)Edaravone should be administered in liaison with a well-trained physician, who is well aware of Edaravone and has enough experience treating for the disease indi-cated.

(2) Prior to the administration of Edaravone, enough ex-planation of the adverse reactions, etc. should be given to the patient or their appropriate proxy consenter on behalf of the patient

(3) After administration, aggravation of acute renal failure or renal impairment, severe liver disorder, and/or disseminated intravascular coagulation (DIC), which can be fatal, may be observed.

(4) Laboratory tests for renal, hepatic function and blood cell counts should be performed in order to detect early changes in BUN, creatinine, AST (GOT), ALT (GPT), LDH, CK (CPK), red blood cell count and platelet count, before or immediately after administration, since the la-boratory data may deteriorate at the early stage of adminis-tration in most cases. During administration, the labor-atory tests should be performed frequently. If abnormal laboratory data and/or symptoms such as oliguria are found, this product should be immediately discontinued and appropriate therapeutic measures should be taken.

(5) Patients with dehydration before administration, showing high BUN/creatinine ratio or other signs, should be care fully monitored systemically during administration, since fatal outcome has been reported in these patients.

(6) Decreased serum creatinine due to ALS. Therefore, time course of serum creatinine level should be monitored to detect deteriorating tendency, instead of comparing serum creatinine value at single point in time with reference value. Since BUN level may fluctuate according to water amount in the body, time course of BUN level should be monitored to detect deteriorating tendency.

(7) In patients during the treatment such as estimated glomerular filtration rate (eGFR) based on serum cystatin C level, calculation of creatinine clearance by urine collection, in addition to measurement of serum creatinine and BUN.

(8) when an antibiotic is coadministered for the treatment of infections during the administration of Edaravone or not . If the administration is continued, laboratory data should be monitored more frequently. After the administration the patient should also be carefully monitored by the frequent laboratory data monitoring.

(9) When renal impairment occurs during administration Edaravone should be immediately discontinued

10) In the patients with infections or with severe disturbance of consciousness. Therefore the risk/benefit evaluation should be carefully carried out for these patients.

(11)The elderly patients should be monitored carefully, since many fatal outcomes have been reported in the patients.

CONTRAINDICATIONS :

(1) Patients with severe renal impairment.

(2) Patients with a history of hypersensitivity to any of the ingredients Edaravone

STORAGE : Store in a cool ,dry place. Protect from light & moisture. Below 25°C

PRESENTATIONS : Edaravone Injection in strength of 30 mg is available in 20 ml Ampoule.

Mfg. by : Pace Biotech
(An ISO 9001 : 2008, GMP & GLP Certified Co.)
Surajpur, Paonta Sahib,
Distt.- Sirmour (H.P.) - 173001

Allegato
AL MINISTERO DELLA SALUTE
USMAF-SASN LOMBARDIA, PIEMONTE E VALLE D'AOSTA
UNITA' TERRITORIALE TORINO CASELLE

Richiesta di importazione di medicinali ai sensi del D.M. 11/02/1997.

Il sottoscritto Dr. .....
Residente in..... via .....
tel.....iscritto nell'Albo dell'Ordine dei Medici-Chirurghi di ..... al n..... cod. regionale.....
..... chiede di importare il medicinale (contenente il seguente/i principio/i attivo/i):.....
nome commerciale: .....
forma farmaceutica .....
nella quantità di numero ..... confezioni contenenti .....
di farmaco cadauna. prodotto dalla ditta: ..... (specificare il nome dell'azienda)
Precisa che tale medicinale è regolarmente registrato nel Paese di provenienza: .....
per il trattamento di .....
Tale medicinale è indispensabile per la cura del Sig. (iniziali o codice) .....
affetto da: .....
Motivo per cui viene richiesta la scorta di reparto****.....

Dichiara altresì che il farmaco:

- non ha valida alternativa terapeutica con altri medicinali registrati in Italia;
- non contiene sostanze stupefacenti o psicotrope;
- non è un emoderivato;
- verrà impiegato sotto la propria diretta responsabilità, dopo aver ottenuto il consenso informato scritto del paziente;
- che le generalità del paziente ed i documenti relativi al consenso informato sono custoditi presso il medico curante per la durata prevista dalla normativa vigente.

Particolari condizioni di conservazione del medicinale:
Temperatura (es. -20°C, da 2 a 8°C, < 25°, <30°, nessuna indicazione): .....
Altro: .....

Luogo e data _____

_____
Timbro e firma leggibile del medico

_____
Timbro e firma leggibile del Servizio Farmaceutico

****Da compilare solo in caso di scorta reparto

Unipharma SA
Via Figino, 6
6917 – Barbengo Lugano – Switzerland
Tel. +41 91 985 62 11
Fax. +41 91 985 62 22
E-mail: sales@unipharma.ch

Cert. N°23997

Offerta cliente

M-COM 05

OFFERTA N°2019-19000088
VALIDA DAL 09.01.2019 AL 10.03.2019

Nr Art	Descrizione	Produttore	Titolare AIC	Origine	Conservazione	gg consegna	Prezzo EUR	Prezzo unitario EUR
74696	Edastar inj 1.5 mg/ml 1 amp 20 ml	BDR Pharmaceuticals Intl Pvt. Ltd.	Lupin Pharmaceuticals Ltd	India	temperatura ambiente	20	5.70	5.70000

Composizione:

Nr Art	Prodotto	DenominazionePrincipale	Dose
74696	Edastar inj 1.5 mg/ml 1 amp 20 ml	Edaravon (ASK;INN.L36.D)	1.5 mg/mL

Costi di spedizione, imballo e sdoganamento:

Corriere	Da Kg	Fino a Kg	Porto EUR
Fisso € 30	0.00	10'000.00	30.00

ALLEGATO N. 3

Unipharma SA
Via Figino, 6
6917 – Barbengo Lugano – Switzerland
Tel. +41 91 985 62 11
Fax. +41 91 985 62 22
E-mail: sales@unipharma.ch

Cert. N°23997

Offerta cliente

M-COM 05

CONDIZIONI DI VENDITA UNIPHARMA SA

Prezzi

Tutti i prezzi comunicati per scritto si intendono in franchi svizzeri (CHF) o EURO, IVA esclusa e non includono il costo dell'imballaggio, del trasporto e dello sdoganamento.
In linea di massima vengono applicati i prezzi riportati nei listini in vigore e nelle offerte salvo variazioni di listino da parte del fornitore principale.

Accettazione degli ordini

Nessun valore minimo economico è richiesto. L'ordine diventa impegnativo solo dopo essere stato accettato da Unipharma tramite conferma d'ordine scritta. Annullamenti o modifiche di ordini già confermati sono possibili solo se comunicati per iscritto all'indirizzo sales@unipharma.ch entro 24 ore dal ricevimento della conferma d'ordine inviata da Unipharma.
Gli ordini vengono accettati con l'indicazione del prezzo in CHF o EURO al cambio concordato.

Fatturazione

Le fatture vengono emesse in CHF/EURO al cambio sopra menzionato.

Termine di consegna

Se un ordine al momento del suo arrivo si riferisce del tutto o in parte a merce non disponibile sarà nostra cura informare di ciò il cliente, avvisandolo dell'avvenuta ordinazione vincolante da parte nostra della merce che verrà riservata a suo nome.
Le spedizioni avvengono

- in giornata per le specialità registrate in Svizzera presso Swissmedic
- entro 20 giorni per le specialità da ordinare all'estero, conformemente alla disponibilità del fornitore principale.

La consegna al vostro domicilio è garantita entro e non oltre 48 ore dalla spedizione.

Trasporto

Le spese di trasporto, se non concordato diversamente, sono a carico del cliente.
I trasporti vengono effettuati secondo le indicazioni delle Aziende produttrici rispettando la catena del freddo, se necessario.

Formalità doganali

Ufficio di entrata della merce: Ciampino o Ponte Chiasso (CO)
La dichiarazione di Nulla osta è da intestare all'Ufficio doganale di sanità aerea di Ciampino.

Consegna della merce

La merce viene consegnata all'indirizzo indicato dal cliente con gli obblighi di dogana ed anticipo IVA e spese di trasporto già assolti.
Per l'IVA a carico del cliente, da noi anticipata e fatturata, sarà rimessa in originale la bolla doganale da allegare ai documenti contabili.

Pagamento

Le fatture devono essere saldate entro 90 giorni dalla data della fattura, versando l'importo sul nostro conto 247-959.570.62J – IBAN CH88 0024 7247 9595 7062J – Swift UBSWCHZH80A presso UBS SA – 6900 Lugano

Garanzia

Per i danni riscontrati all'arrivo dev'essere fatta riserva al vettore. Altri danni (difetti del materiale, consegna errata o quantità mancanti) devono esserci comunicati entro 8 giorni dal ricevimento della merce. I reclami avanzati oltre tale termine non potranno più essere presi in considerazione. La nostra responsabilità cessa alla consegna del prodotto.
Escludiamo ogni responsabilità per danni causati alle persone, alle cose o ai beni dall'utilizzo della merce oggetto della fornitura. Sono escluse le richieste di risarcimento di clienti o terzi destinate a riparare eventuali danni causati dall'utilizzo della merce oggetto dei fornitura, quindi di null'altro – in particolare secondo i principi di responsabilità del prodotto – salvo diversamente prescritto per legge.

Ritorni

Ritorni di merce sono accettati solo se preventivamente concordati.

Richiamo del prodotto

In caso di ritiro di specialità o di un lotto per ragioni di sicurezza da parte del fabbricante, il cliente viene immediatamente informato. Il cliente dovrà comunicare ad Unipharma il numero di pezzi giacenti presso i propri magazzini e procedere al reso entro 7 giorni dal ricevimento dell'avviso di richiamo. A ricevimento della merce verrà emessa nota di credito.

Foro competente

Per qualsiasi controversia, se non diversamente concordato, viene applicato il Diritto Svizzero: il foro competente è quello di Lugano.

For the use of Neurologist or a Hospital or Institution only.

Edaravone Injection JP 1.5 mg/ml

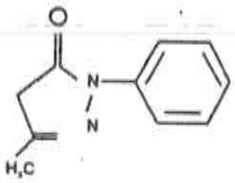
Edastar

Dosage Form:
Injection for Intravenous infusion

Composition:
Each ml contains:

Edaravone JP	1.5 mg
Water for Injections IP	q.s.

Description:
Edaravone ,3-methyl-1-phenyl-2-pyrazolin-5-one, is a potant scavenger of free radicals



Clinical Pharmacology:
Edaravone scavenges free radicals and inhibits lipid peroxidation and thereby prevents oxidative damage to brain cells (vascular endothelial cells/nerve cells).

Mechanism of Action
Free radicals such as hydroxyl radical (OH) play a major causative role in the development of cerebral vascular accident resulting from ischemia. In the event of ischemia or at the time of blood reperfusion following ischemia, the hyperactivity of a metabolic system of arachidonic acid, etc. precipitates the production of free radicals. These free radicals can damage cell membranes by promoting peroxidation of cell membrane lipids, which leads to cell membrane injury and ultimately to cerebral function impairment.

Edaravone scavenges free radicals and possess an inhibitory effect against lipid peroxidation, and thereby suppresses damage to brain cells (vascular endothelial cells/neuron cells) due to oxidation. In other words, edaravone protects the brain in case of acute ischemic stroke by exerting its inhibitory effects against the development and progression (exacerbation) of ischemic cerebral cascular accidents such as cerebral edema, cerebral infarction, neurological deficits and delays neuron cell death.

Pharmacokinetics
Healthy male adults and healthy old males were involved to evaluate pharmacokinetic parameters.

The drug was administered (0.5 mg/kg) over 30 minutes twice a day for 2 days to 5 healthy volunteers and 5 healthy old males.

The Cmax (mg/ml), t1/2α (h) and t1/2β (h) observed in healthy male adults and elderly males in the almost same way without any signs of accumulation.

The plasma unchanged drug concentration disappeared in both healthy adults and elderly males in the almost same way without any signs of accumulation.

The binding rates of edaravone (5 μM and 10 μM) to human serum protein and human serum protein albumin were 92% and 89-91% respectively (in vitro).

The major metabolite in healthy male adults and healthy elderly males was sulfate conjugate in plasma, and glucuronide conjugate was also detected in plasma. In urine, the major metabolite of edaravone was glucuronide conjugate and sulfate conjugate was also detected. 0.7-0.9% and 71-79.9% of the dose was recovered as unchanged drug and metabolites in urine, respectively, upto 12 hours after each dose.

Indications:
Edastar is indicated for the improvement of neurological symptoms, disorder of activities of daily living, and functional disorder associated with acute ischemic stroke.

Dosage and Administration:
Edaravone injection is for intravenous infusion only. Not for Bolus injection. Each ampoule is for single use only.

The usual adult dose is one ampoule (30 mg)diluted with an appropriate saline, which is administered over 30 minutes twice a day in the morning and the evening. Administration of this product should be initiated within 24 hours after the onset of the disease, and the duration of administration should be within 14 days.

It should be considered that the duration of administration is reduced according to the patient's clinical condition.

Elderly: If any adverse reactions are observed, the drug should be discontinued and appropriate therapeutic measures should be taken as the physiological functions are diminished in elderly patients. Special caution should be exercised as many fatal cases have been reported in these patients.

Pediatric use: The safety of edaravone has not been established in children.

Hepatic impairment: The major adverse effect associated with edaravone administration is hepatic dysfunction. So caution should be exercised when edaravone will be administered in the patients with hepatic dysfunction. Liver function tests should be performed frequently and patients should be monitored carefully. Abnormal changes in laboratory test values were reported. The major abnormal changes were abnormal liver function test with increased AST (GOT) and increased ALT (GPT).

Renal impairment; Caution is advised when edaravone is administered in the patients with renal function disorder since acute renal failure or renal impairment may be aggravated. The drug is contraindicated in the patients with severe renal impairment.

Contra-Indications:
- Patients with severe renal function disorder as the renal function disorder may be aggravated.
- Patients with a history of hypersensitivity of drug or its any ingredient.

Warnings and Precautions:
For I.V. infusion only.

This product should be administered in liaison with a well trained physician, who is well aware of this drug and has enough experience treating for ischemic stroke.
Prior to the administration of this product, enough explanation of the adverse reaction, etc. should be given to the patients or their appropriate proxy consenter on behalf of the patient.

After administration of edaravone, aggravation of acute renal failure or renal failure or renal impairment, severe liver disorder and/or disseminated intravascular coagulation (DIC), which can be fatal, may be observed. Among these patients serious cases of concurrently developing renal impairment, hepatic impairment and /or hematological disorders etc have been reported. When renal impairment occurs during administration, edaravone should be immediately discontinued and appropriate therapeutic measures should be taken, in liaison with a physician with enough knowledge and experience treating for renal failure.

Patients with dehydration before administration, showing high BUN/creatinine ratio or other signs, should be carefully monitored systematically during administration, since fatal outcome has been reported in these patients.

Caution is advised in patients with infections since acute renal failure or renal impairment may be aggravated due to the deterioration of systemic conditions. It should be carefully considered whether to continue edaravone administration when antibiotics will be prescribed to treat infections, as chances of renal impairment may enhance. If the administration is continued, laboratory data should be monitored more frequently.

In the patients with infections or with severe disturbance of consiousness many fatal cases have been reported. Therefore the risk/benefit evaluation should be carefully carried out for these patients.

Laboratory tests for renal, hepatic function and blood cell counts should be performed in order to detect early changes in BUN, creatitine, LDH, CK (CPK), red blood cell count and platelet count, before administration, since the laboratory data may deteriorate at the early stage of administration in most cases. During administration, the laboratory tests should be performed frequently. If abnormal laboratory data and/or symptoms such as oliguria are found, this product should be immediately discontinued and appropriate therapeutic measures should be taken. Careful monitoring should be continued after the discontinuation of this product as well.

Hematogical tests should be performed frequently and patients should be monitored carefully, since thrombocytopenia or granulocytopenia and disseminated intravascular coagulation (DIC) may occur. Edaravone should be discontinued and appropriate therapeutic measures, including administration of corticosteroids, should be taken, when any abnormalities are found.

Patients should be monitored carefully, since acute lung injury with pyrexia, cough, dyspnea and chest X-ray abnormality may occur. Edaravone should be discontinued and appropriate therapeutic measures, including administration of corticosteroids, should be taken, when any signs of acute

lung injury are found.
Patients should be monitored carefully, since rhabdomyolysis may occur. Edaravone should be discontinued and appropriate therapeutic measures should be taken, when myalgia, weakness, increased CK (CPK) and increased blood and/or urine myoglobin are found.

If shock or anaphylactoid reactions (urticaria, decreased blood pressure and dyspnea etc.) is observed, edaravone should be discontinued.

Caution is advised in patients with hepatic function disorder. Liver function tests should be performed and patients should be monitored carefully, since severe hepatitis including fulminant hepatitis, hepatic dysfunction or jaundice with significant increase in AST (GOT), ALT (GPT), A1-P, gamma-GTP, LDH, blood bilirubin etc may occur. Edaravone should be discontinued and appropriate therapeutic measures should be taken, when any abnormalities are found.

Caution is advised in patients with cardiac disorder. The cardiac diseases may be aggravated and renal impairment may also occur.

The elderly patients should be monitored carefully, since many fatal outcomes have been reported in the patients.
It has been reported that cerebral embolism reoccurred or cerebral hemorrhage occurred during or after administration of edaravone. So effects should be monitored when edaravone is prescribed in the patients.

Pregnancy & Lactation
Safety of Edaravone in pregnant women has not been established. Edaravone is not recommended to be administered in pregnant women or women who may possibly be pregnant.

Side effects:
Thirty adverse reactions due to this product were reported in 26 of 569 patients (4.57%). The main adverse reactions were hepatic dysfunction in 16 patients (2.81%) and rash in 4 patients (0.70%). Also, abnormal changes in laboratory test values were reported in 122 of 569 patients (21.4%). The major abnormal changes were abnormal liver function test with increased AST (GOT) in 43 of 558 patients (7.71%) and increased ALT (GTP) in 46 of 559 patients (8.23%) (in the clinical studies before the approval).

Acute renal failure, hepatic dysfunction, nephritic syndrome, hepatitis, jaundice, thrombocytopenia, granulocytopenia, disseminated intravascular coagulation (DIC), acute lung injury, rhabdomyolysis, shock, anaphylactoid reaction (urticaria, decreased blood pressure and dyspnea) were also reported.

The other adverse effects reported are:

Incidence/Type	≥ 5%	≥ 0.1%	Incidence Unknown
Hypersensitivity		Redness, swelling, wheals, pruritus	Erythema (erythema Multiforme exsudativum, etc.)
Hematologic		Decreased red blood cell Count, increased white blood cell count, decreased white blood cell count, decreased Hematocrit, decreased Hemoglobin, increased Platelet count, decreased platelet count	
Injection site		injection site rash, injection site redness and swelling	
Hepatic	Increased AST (GOT), increased ALT (GPT), increased LDH, increased Al-P, Increased λ-GTP	Increased total bilirubin, urobilinogen appeared, bilirubinuria	
Renal		Increased BUN, increased serum uric acid, Proteinuria, hematuria	Increased creatinine
Gastrointestinal		Nausea	Vomiting
Others		Pyrexia, feeling hot, increased serum cholesterol Decreased serum cholesterol, increased triglyceride, decreased serum total protein, increased CK (CPK), decreased CK (CPK), decreased Serum Potassium, decreased Serum calcium	Headache, increased serum potassium

Overdose:
No data is available on overdosage with edaravone injection.

Preparation and Administration:
Edaravone injection should be diluted with physiological saline. If edaravo would be diluted with any other infusion fluids including saccharides, t concentration of edaravone may decrease with time.

Edaravone injection should not be mixed with total parental nutriti preparations and/or amino-acid infusions before administration. edaravone will be administered with these preparations, the concentration the drug may decrease with time.

Incompatibilities:
Edaravone injection should not be administered with infusion anticonvulsant drugs like diazepam, phenytoin sodium, etc. and not mixed with potassium canrenoate as the solution may become cloud administered together.

Edaravone injection should be diluted with physiological saline. If edaravo would be diluted with any other infusion fluids including saccharides, t concentration of edaravone may decrease with time.

Edaravone injection should not be mixed with total parental, nutriti preparations and /or amino-acid infusions before administration. edaravone will be administered with these preparations, the concentration the drug may decrease with time.

Storage & Handling:
Store below 25°C.
Keep out of reach of children.

Expiry Date:
Refer product label for expiry date. Do not use after expiry date.

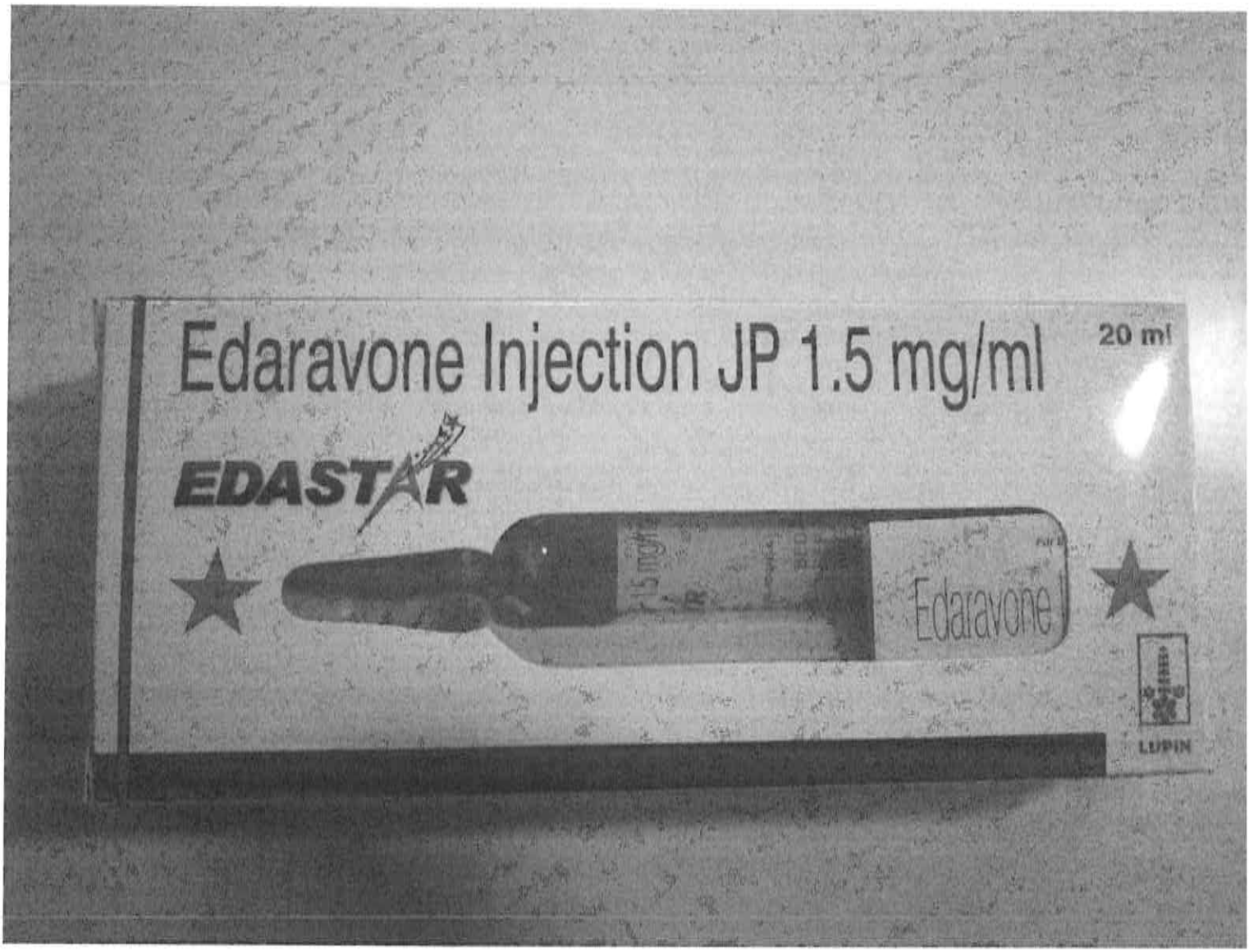
Presentation:
Edastar is available as 1.5 mg/ml in 20 ml ampoule.

To report product complaint or Adverse Drug reaction dial Toll Free no.: 1800-209-2505

For further details, please write to:

Manufactured in India by:
BDR Pharmaceuticals Intl Pvt. Ltd.
At : Plot No. J-174, J-168, J-168/1,
MIDC, Tarapur, Boisar, Dist. Thane - 401 506.

Marketed by :
LUPIN LTD.
159, C.S.T. Road, Kalina,
Santacruz (East),
Mumbai - 400 098, INDIA.


Edaravone Injection JP 1.5 mg/ml
20 ml
EDASTAR
Edaravone
LUPIN

REGIONE CAMPANIA
AZIENDA OSPEDALIERA DI CASERTA
SANT'ANNA E SAN SEBASTIANO
DI RILIEVO NAZIONALE E DI ALTA SPECIALIZZAZIONE

DETERMINA DIRIGENZIALE

PARERE CONTABILE

Registro Autorizzazioni n°:	UFFAUT	del	
Budget Economico:	2019		
Codice Conto:	5010101010		
Descrizione:	PROD.FARMAC. CON AIC. ECCEZ.VACCINI-EMODERIVATI REG.		
Presente Autorizzazione:	€3.042,60	n°	SUB
Registro Autorizzazioni n°:		del	
Budget Economico:			
Codice Conto:			
Descrizione:			
Presente Autorizzazione:	€0,00	n°	SUB
Registro Autorizzazioni n°:		del	
Budget Economico:			
Codice Conto:			
Descrizione:			
Presente Autorizzazione:	€0,00	n°	SUB

Caserta, li 22/01/2019

UOC GESTIONE ECONOMICO FINANZIARIA E DELLA

CHIANESE EDUARDO

Il presente atto, in formato digitale e firmato elettronicamente, costituisce informazione primaria ed originale ai sensi dei combinati disposti degli artt. 23-ter, 24 e 40 del D.Lgs. n. 82/2005. Eventuale riproduzione analogica, costituisce valore di copia semplice a scopo illustrativo.

REGIONE CAMPANIA
AZIENDA OSPEDALIERA DI CASERTA
SANT'ANNA E SAN SEBASTIANO
DI RILIEVO NAZIONALE E DI ALTA SPECIALIZZAZIONE

Determina Dirigenziale N. 28 del 25/01/2019

PROPONENTE: **UOC PROVVEDITORATO ED ECONOMATO**

OGGETTO: **Procedura negoziata, ai sensi dell'art.36 D.Lgs. n.50/2016, per l'affidamento della fornitura di n.480 fiale di Edavarone – CIG Z8C26C6D8D**

In pubblicazione dal 25/01/2019 e per il periodo prescritto dalla vigente normativa in materia (art.8 D.Lgs 14/2013, n.33 e smi)

Atto immediatamente esecutivo

UOC AFFARI GENERALI

Direttore Eduardo Chianese

Elenco firmatari

Di Sano Marisa - UOC PROVVEDITORATO ED ECONOMATO

Eduardo Chianese - UOC GESTIONE ECONOMICO FINANZIARIA E DELLA PROGETTUALITA' EUROPEA

Per delega del Direttore della UOC AFFARI GENERALI E LEGALI, il funzionario Gabriella Perrotta

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