SISTEMA SANITARIO REGIONALE
AZIENDA OSPEDALIERA SAN CAMILLO FORLANINI

REGIONE LAZIO

Deliberazione N. 0000495 del 26/03/2024

Struttura Proponente: UOC Acquisizione Beni e Servizi

Centro di costo: A0RZ21JC1S Proposta: 0000444 del 08/03/2024

Oggetto:
ACQUISTO ALL'ESTERO DEL PRINCIPIO ATTIVO LOMUSTINA COMPRESSE 40MG NON COMMERCIALIZZATO IN ITALIA, INDISPENSABILE ALLE ESIGENZE DI UN PAZIENTE AFFETTO DA GLIOMA AD ALTO GRADO PER LE NECESSITA' DELL'ANNO 2024 DELL'AZIENDA OSPEDALIERA SAN CAMILLO- FORLANINI.

IL DIRETTORE GENERALE (*)
Narciso Mostarda

L'Estensore: ***Monica Tanturli*** *Data* 08/03/2024

Il Responsabile del Budget: ***Assunta Caiazza*** *Data* 14/03/2024

Il Dirigente e/o il Responsabile del procedimento con la sottoscrizione della proposta, a seguito dell'istruttoria effettuata, attestano che l'atto è legittimo nella forma e nella sostanza.

Il Responsabile del Procedimento: ***Paolo Farfusola*** *Data* 15/03/2024

Il Direttore della Struttura Proponente: ***Paolo Farfusola*** *Data* 15/03/2024

Il Dirigente Addetto al Controllo di Gestione: ***Miriam Piccini*** *Data* 18/03/2024

Conto Economico/Patrimoniale su cui imputare la spesa: ***Vedere Allegato Assunzione Autorizzazione***

Direttore Amministrativo: ***Paola Longo*** *Data* 20/03/2024

Parere: ***FAVOREVOLE***

Direttore Sanitario: ***Gerardo De Carolis*** *Data* 21/03/2024

Parere: ***FAVOREVOLE***

Hash proposta: 141bce926324c82f594f6579d2d564cf456f97b0fc2411cf4596add2b04c92bd

IL DIRETTORE U.O.C. ACQUISIZIONE BENI E SERVIZI

VISTI il D. Leg.vo n. 502 del 30/12/92 e successive modifiche ed integrazioni, recante norme sul "Riordino della disciplina in materia sanitaria, a norma dell'art.1 della L. n. 421 del 23/10/92";

la L.R. n. 18 del 16/06/94 e successive modifiche ed integrazioni recante "Disposizioni per il riordino del Servizio Sanitario Regionale ai sensi del D. Leg.vo n. 502/92 e successive modifiche ed integrazioni – Istituzione delle Aziende Unità Sanitarie Locali e delle Aziende Ospedaliere";

la L.R. n. 45 del 31/10/96 recante "Norme sulla gestione contabile e patrimoniale delle Aziende Unità Sanitarie Locali e delle Aziende Ospedaliere";
la L. n. 213 del 30/12/2023: Bilancio di previsione dello Stato per l'anno finanziario 2024 e bilancio pluriennale per il triennio 2024 - 2026;

la L.R. n. 23 del 29/12/2023: Legge di stabilità regionale 2024;

la L.R. n. 24 del 29/12/2023: Bilancio di previsione finanziario della Regione Lazio 2024-2026;

il D. Leg.vo n. 36 del 31 Marzo 2023: Codice dei contratti pubblici in attuazione dell'articolo 1 della Legge 21 Giugno 2022, n. 78, recante delega al Governo in materia di contratti pubblici;

PREMESSO - che la Regione Lazio, nelle diverse gare centralizzate effettuate per l'approvvigionamento di medicinali, non ha aggiudicato i farmaci privi di A.I.C., acquisibili solo sul mercato estero, e che l'Azienda Ospedaliera non può interrompere la somministrazione di tali farmaci ai pazienti per non incorrere in interruzione di pubblico servizio;

- che, con nota n. documento 31980/2024 del 16/02/2024, la Farmacia aziendale ha trasmesso la richiesta di acquisto del principio attivo Lomustina compresse 40 mg, privo di A.I.C. e non in commercio in Italia pertanto acquisibile solo all'estero, importato da più Ditte autorizzate, indicandone le quantità per le necessità di trattamento di un paziente affetto da malattia oncologica fino al 31/12/2024 (all. 1);

- che sono state richieste offerte economiche alle Ditte Farmaceutica Internazionale Italiana, Mondial Pharma, Ottopharma, Profarma Italia, Import Pharma, Unipharma, Inter Farmaci Italia, e che le stesse sono tutte pervenute ad eccezione di quelle delle Ditte Profarma Italia, Import Pharma, Unipharma e Inter Farmaci Italia (all. 2);

PRESO ATTO che il prezzo più basso risulta essere quello proposto dalla Ditta Ottopharma ad € 1,0166/cpr. (confezioni da 6 compresse) + € 18,00 per ciascuna spesa di trasporto, con spese di importazione gratuite;

RITENUTO pertanto necessario, ai sensi dell'art. 108, co. 3, del D. Leg.vo n. 36 del 31/03/2023, procedere all'acquisto all'estero presso la Ditta Ottopharma del principio attivo di che trattasi, nella quantità di 42 compresse (confezioni da 6 compresse) e 2 trasparti per un totale di € 42,70 + Iva 10% + € 18,00 a trasporto (CIG B0B1BDD62E);

RITENUTO opportuno nominare quale Responsabile del Progetto il Direttore della U.O.C. Acquisizione Beni e Servizi, Dott. Paolo Farfusola e quale Direttore dell'Esecuzione del Contratto la farmacista della U.O.C. Farmacia aziendale D.ssa Elena Compagnucci;

TENUTO CONTO che, ai sensi dell'art. 28 del D.Leg.vo n. 36/2023, verrà pubblicato sull'apposito sito aziendale l'avviso per la trasparenza;

RILEVATO che la spesa complessiva corrispondente ad € 78,70 + Iva 10%, pari ad € 86,57 compresa Iva, è da imputare sui conti economici nn. 501010113000 e 502020107000 del piano dei conti di contabilità economico patrimoniale, anno 2024, Centro di Costo SOFA01F01P, aut. 3, nel modo seguente:
Conto economico 501010113000 € 46,97 c/Iva
Conto economico 502020107000 € 39,60 c/Iva

ATTESTATO che il presente provvedimento, a seguito dell'istruttoria effettuata, nella forma e nella sostanza è totalmente legittimo, ai sensi e per gli effetti di quanto disposto dall'art. 1 della Legge 20/94 e successive modifiche, nonché alla stregua dei criteri di economicità e di efficacia di cui all'art. 1, co. 1, della Legge 241/90, come modificato dalla Legge 15/2005;

PROPONE

- di acquistare sul mercato estero presso la Ditta Ottopharma, ai sensi dell'art. 50 del D. Leg.vo n. 36/2023, il principio attivo Lomustina compresse 40 mg. nella quantità di n. 42 compresse (confezione da 6 compresse) al prezzo di € 6,10/conf. + € 18,00 a trasporto con spese di importazione gratuite, per le necessità di trattamento di un paziente affetto da malattia oncologica dell'Azienda Ospedaliera San Camillo Forlanini fino al 31/12/2024 (CIG B0B1BDD62E);

- di nominare quale Responsabile del Progetto il Direttore della U.O.C. Acquisizione Beni e Servizi, Dott. Paolo Farfusola e quale Direttore dell'Esecuzione del Contratto la D.ssa Elena Compagnucci della U.O.C. Farmacia aziendale;

- di pubblicare sull'apposito sito aziendale, ai sensi dell'art. 28 del D.Leg.vo n. 36/2023, l'avviso per la trasparenza;

- di stabilire che la spesa complessiva corrispondente ad € 78,70 + Iva 10%, pari ad € 86,57 compresa Iva, sia imputata sui conti economici nn. 501010113000 e 502020107000 del piano dei conti di contabilità economico patrimoniale, anno 2024, Centro di Costo SOFA01F01P, aut. 3, nel modo seguente:
Conto economico 501010113000 € 46,97 c/Iva
Conto economico 502020107000 € 39,60 c/Iva

- di corrispondere il dovuto alla Ditta fornitrice nei limiti del suddetto importo, ad avvenuta esecuzione della fornitura regolarmente effettuata, previa presentazione di appositi documenti contabili conformi alla vigente normativa fiscale.

IL DIRETTORE U.O.C. ACQUISIZIONE BENI E SERVIZI
(DOTT. PAOLO FARFUSOLA o suo sostituto)

IL DIRETTORE GENERALE

VISTE le deliberazioni della Giunta Regionale Lazio n. 5163 del 30/06/1994 e n. 2041 del 14/03/1996;

VISTO l'art. 3 del decreto legislativo 30.12.92 n. 502 e successive modificazioni ed integrazioni, nonché l'art. 9 della L.R. n. 18/94;

VISTO il decreto del Presidente della Regione Lazio n. T00198 del 28 ottobre 2021;

VISTA la propria deliberazione n. 1523 del 2 novembre 2021;

LETTA la proposta di deliberazione: "Acquisto all'estero del principio attivo Lomustina compresse 40mg non commercializzato in Italia, indispensabile alle esigenze di un paziente affetto da Glioma ad alto grado per le necessita' dell'anno 2024 dell'Azienda Ospedaliera San Camillo- Forlanini" presentata dal Direttore U.O.C. Acquisizione Beni e Servizi;

PRESO ATTO che il Dirigente proponente il presente provvedimento, sottoscrivendolo, attesta che lo stesso, a seguito dell'istruttoria effettuata, nella forma e nella sostanza è totalmente legittimo, ai sensi dell'art. 1 della Legge 20/1994 e successive modifiche, nonché alla stregua dei criteri di economicità e di efficacia di cui all'art. 1, primo comma, della Legge 241/90, come modificato dalla Legge 15/2005;

VISTI i pareri favorevoli del Direttore Amministrativo e del Direttore Sanitario;

DELIBERA

di adottare la proposta di deliberazione di cui sopra e, conseguentemente:

- di acquistare sul mercato estero presso la Ditta Ottopharma, ai sensi dell'art. 50 del D. Leg.vo n. 36/2023, il principio attivo Lomustina compresse 40 mg. nella quantità di n. 42 compresse (confezione da 6 compresse) al prezzo di € 6,10/conf. + € 18,00 a trasporto con spese di importazione gratuite, per le necessità di trattamento di un paziente affetto da malattia oncologica dell'Azienda Ospedaliera San Camillo Forlanini fino al 31/12/2024 (CIG B0B1BDD62E);

- di nominare quale Responsabile del Progetto il Direttore della U.O.C. Acquisizione Beni e Servizi, Dott. Paolo Farfusola e quale Direttore dell'Esecuzione del Contratto la D.ssa Elena Compagnucci della U.O.C. Farmacia aziendale;

- di pubblicare sull'apposito sito aziendale, ai sensi dell'art. 28 del D.Leg.vo n. 36/2023, l'avviso per la trasparenza;

- di stabilire che la spesa complessiva corrispondente ad € 78,70 + Iva 10%, pari ad € 86,57 compresa Iva, sia imputata sui conti economici nn. 501010113000 e 502020107000 del piano dei conti di contabilità economico patrimoniale, anno 2024, Centro di Costo SOFA01F01P, aut. 3, nel modo seguente:

Conto economico 501010113000 € 46,97 c/Iva
Conto economico 502020107000 € 39,60 c/Iva

- di corrispondere il dovuto alla Ditta fornitrice nei limiti del suddetto importo, ad avvenuta esecuzione della fornitura regolarmente effettuata, previa presentazione di appositi documenti contabili conformi alla vigente normativa fiscale.

La struttura complessa proponente curerà gli adempimenti consequenziali del presente provvedimento.

Il presente atto è pubblicato nell'Albo dell'Azienda nel sito internet aziendale www.scamilloforlanini.rm.it *per giorni 15 consecutivi, ai sensi della Legge Regionale 31.10.1996 n. 45.*

IL DIRETTORE GENERALE
(DOTT. NARCISO MOSTARDA o suo sostituto)

AZIENDA OSPEDALIERA
SAN CAMILLO FORLANINI

U.O.C. FARMACIA

Circ.one Gianicolense 87- 00152 -Roma

All. 1

Prot: 41 /F

Roma, 16/02/2024

16/02/2024

Documento N. 31980/2024

Direzione
Acquisizione Beni e Servizi

Dott. Farfusola

Oggetto: Acquisto all'estero principio attivo Lomustina capsule da 40 mg

Si inoltra la richiesta d'acquisto per il farmaco Lomustina 40 mg come da richiesta dell'UOC di Oncologia per le necessità di trattamento di un paziente affetto da Glioma ad alto grado.

Il farmaco non è commercializzato in Italia, pertanto si indicano i nomi delle società presso cui richiedere l'offerta:

Interfarmaci

(Intercompany) NON + ESISTENTE

Unipharma

Farmacia Internazionale Italiana

Profarma Italia

Ottopharma

Per l'anno 2024 sono previste 40 compresse.

Il fabbisogno deve essere contabilizzato sul C.E. 501010113000 MEDICINALI ESTERI Autorizzazione 3.

Il trasporto per farmaci esteri può essere contabilizzato per n. 2 trasporti sul C.E. 502020107000.

La Dott.ssa E. Compagnucci può essere indicata come DEC ai fini dell'adesione.

Cordiali saluti

Dott.ssa L. Lombardozzi

Dott.ssa E. Compagnucci

Richiesta farmaci schema PCV Sig. D. M.

Sara Ramponi

mar 06/02, 15:37

Elena Compagnucci;Carlo Garufi;Barbara De Luca

Si richiedono Lomustina 120 mg giorno 1, Procarbazina 100 mg/die giorni da 8 a 21, ogni 6 settimane per ilSig. D. M., nato il 2/1/1968, affetto da glioma ad alto grado

Sono previsti sei cicli di trattamento.

Cordiali saluti

Sara Ramponi

OttoPharma

PROPOSTA DI FORNITURA

Spett.le

AZIENDA OSPEDALIERA SAN CAMILLO
FORLANINI
CIRC. GIANICOLENSE, 87

152 ROMA RM

N°	Data	Cliente	Pag.
41172	**27/02/24**	**81**	**1**

Spedizione	Porto	Pagamento
A MEZZO CORRIERE	FRANCO	60 GG BONIFICO D.F.

CODICE ARTICOLO	DESCRIZIONE ARTICOLO	PRODUTTORE E TITOLARE AIC	PROVENIENZA	PREZZO UNITARIO	PREZZO CONFEZIONE	SPESE TRASPORTO	TEMPI DI CONSEGNA	NOTE
FAR1582	LOMOOTHER 40MG 6 CPR (LOMUSTINA)	THERDOSE PHARMA	INDIA	1,016666	6,10	18,00	10-12 GG LAVORATIVI	
					da 6 cp			
					(7 cpr.)			

OTTOPHARMA srl
UFFICIO OFFERTE
Marco Albertini

Tutti i prezzi sono da intendersi I.V.A. 10% esclusa - Spese di importazione: GRATUITE >>Valida fino al 31/12/24 << (Salvo aumenti disposti dalla ditta produttrice.)

In considerazione dell'attuale scenario economico e politico, per cause non direttamente imputabili a Ottopharma, i tempi di consegna potrebbero subire ritardi e alle spese di trasporto potrebbero essere applicate, senza necessità di preavviso, maggiorazioni.

OTTOPHARMA S.r.l.
Sede Operativa: Via Barro, 76/F - 28045 Invorio (NO) Tel: 0322/255639 Fax: 0322/060732 - P.IVA - C.F. 02457060032
| www.ottopharma.com | info@ottopharma.com

LOMUSTINE
CAPSULES 10 mg,
40 mg, 100 mg

Rx only

LOMOOTHER 10, 40, 100

COMPOSITION:

LOMOOTHER 10

Each capsule contains:

Lomustine	10 mg
Excipients	q.s.

Colour: approved colours used in capsule shell

LOMOOTHER 40

Each capsule contains:

Lomustine	40 mg
Excipients	q.s.

Colour: approved colours used in capsule shell

LOMOOTHER 100

Each capsule contains:

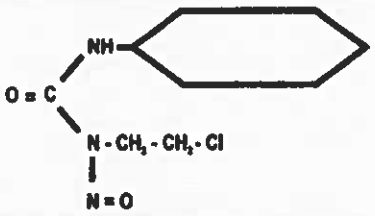
Lomustine	100 mg
Excipients	q.s.

Colour: approved colours used in capsule shell

DESCRIPTION:

Lomustine is an alkylating drug for oral administration. The chemical name for lomustine is 1-(2-chloro-ethyl)-3-cyclohexyl-1-nitrosourea and the molecular formula is $C_9H_{16}ClN_3O_2$. The molecular weight is 233.71. Lomustine is a yellow powder, which is soluble in 10% ethanol (0.05 mg per mL) and in absolute alcohol (70 mg per mL). Lomustine is insoluble in water(<0.05 mg per mL).

The chemical structure is:



Lomustine Capsules is supplied as 10 mg, 40 mg, and 100 mg capsules and contains the following inactive ingredients: magnesium stearate and mannitol. The capsule shells are composed of gelatin and coloring pigments, depending on the strength: titanium dioxide, and/or yellow iron oxide, and/or Indigo tine – FD&C Blue2.

INDICATIONS AND USAGE:

Brain Tumors

Lomustine Capsules is indicated for the treatment of patients with primary and metastatic brain tumors following appropriate surgical and/or radiotherapeutic procedures.

Hodgkin's Lymphoma

Lomustine Capsules is indicated as a component of combination chemotherapy for the treatment of patients with Hodgkin's lymphoma whose disease has progressed following initial chemotherapy.

DOSAGE AND ADMINISTRATION:

Important Prescribing and Dispensing Information

PRESCRIBE ONLY ONE DOSE FOR EACH TREATMENT CYCLE. DO NOT DISPENSE ENTIRE CONTAINER.

Dispense only a sufficient number of capsules for one dose.

Confirm the total dose prescribed by the physician and the appropriate combination of capsule strengths.

Dispense only the appropriate number of Lomustine Capsules required for the administration of a single dose.

The prescribed dose may consist of two or more different strengths and colors of capsules.

Instruct patients that Lomustine Capsules is taken as a single oral dose and will not be repeated for at least 6 weeks.

Taking more than the recommended dose causes toxicities, including fatal outcomes [see Warnings and Precautions and Overdosage]

Lomustine Capsules is a cytotoxic drug. Follow applicable special handling and disposal procedures.

To minimize the risk of dermal exposure, always wear impervious gloves when handling bottles containing Lomustine Capsules. Do not break Lomustine Capsules; avoid exposure to broken capsules. If dermal contact occurs, wash areas of skin contact immediately and thoroughly.

Recommended Dose

The recommended dose of Lomustine Capsules in adult and pediatric patients is 130 mg/m^2 taken as a single oral dose every 6 weeks. Round doses to the nearest 5 mg. Give as a single oral dose and do not repeat for at least 6 weeks. Reduce dose to 100 mg/m^2 every 6 weeks in patients with compromised bone marrow function. Also reduce dose accordingly when using with other myelosuppressive drugs.

Dose Modifications

Perform weekly complete blood counts and withhold each subsequent dose for more than 6 weeks if needed until platelet counts recover to 100,000/mm^3 or greater and leukocytes recover to 4000/mm^3 or greater [see Warnings and Precautions]

Modify each dose of Lomustine Capsules according to the hematologic response of the preceding dose as described in Table 1:

Table 1. Dose Modifications for Lomustine Capsules

Nadir after Prior Dose		Dose Adjustment
Leukocytes (/mm^3)	Platelets (/mm^3)	
≥ 4000	≥ 100,000	None
3000 – 3999	75,000 – 99,999	None
2000 – 2999	25,000 – 74,999	Reduce dose by 30%
< 2000	< 25,000	Reduce dose by 50%

WARNINGS AND PRECAUTIONS:

Delayed Myelosuppression

Lomustine Capsules causes myelosuppression that can result in fatal infections and bleeding. Myelosuppression from Lomustine Capsules is delayed, dose-related, and cumulative. It usually occurs 4 to 6 weeks after drug administration and persists for 1 to 2 weeks. Thrombocytopenia is generally more severe than leukopenia. Cumulative myelosuppression from Lomustine Capsules is manifested by greater severity and longer duration of cytopenias.

Monitor blood counts for at least 6 weeks after each dose. Do not give Lomustine Capsules more frequently than every 6 weeks. Adjust dose based on nadir blood counts from prior dose [see Dosage and Administration)

Risk of Overdosage

Fatal toxicity occurs with over dosage of Lomustine Capsules. Dispensing or administering more than one dose can lead to fatal toxicity.

Prescribe only one dose at a time. Dispense only enough capsules for one dose. Both physician and pharmacist should emphasize to the patient that only one dose of Lomustine Capsules is taken every 6 weeks [see Dosage and Administration and Overdosage

Pulmonary Toxicity

Pulmonary toxicity characterized by pulmonary infiltrates

and/or fibrosis occurs with Lomustine Capsules . Patients with a baseline below 70% of the predicted Forced Vital Capacity (FVC) or Carbon Monoxide Diffusing Capacity (DLCO) are at increased risk. The onset of pulmonary toxicity occurs after an interval of 6 months or longer from the start of therapy, with cumulative doses of Lomustine Capsules usually greater than 1100 mg/m^2.
Obtain baseline pulmonary function tests prior to initiating treatment and repeat frequently during treatment. Permanently discontinue Lomustine Capsules in patients diagnosed with pulmonary fibrosis.

Secondary Malignancies
Secondary malignancies, including acute leukemia and myelodysplasia, occur with long term use.

Hepatotoxicity
Hepatic toxicity, manifested by increased levels of transaminases, alkaline phosphatase, and bilirubin occurs with Lomustine Capsules.
Monitor liver function.

Nephrotoxicity
Progressive renal failure with a decrease in kidney size occurs with Lomustine Capsules.
Monitor renal function.

Embryo-Fetal Toxicity
Based on animal data and its mechanism of action, Lomustine Capsules can cause fetal harm when administered to a pregnant women. Embryo-fetal toxicity and teratogenicity occurred in rats and rabbits receiving lomustine daily during organogenesis at doses approximately two to four times the total human dose of 130 mg/m^2 over 6 weeks (0.18 to 0.27 times the single human dose of 130 mg/m^2) based on body surface area (BSA). Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with Lomustine Capsules and for 2 weeks after the final dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with Lomustine Capsules and for 3.5 months after the final dose

CONTRAINDICATIONS:
None.

ADVERSE REACTIONS:
The following serious adverse reactions are discussed in greater detail in other sections of the labeling:
- Delayed myelosuppression [see Warnings and Precautions]
- Risks of overdosage [see Warnings and Precautions]
- Pulmonary toxicity [see Warnings and Precautions]
- Secondary malignancies [see Warnings and Precautions]
- Hepatotoxicity [see Warnings and Precautions]
- Nephrotoxicity [see Warnings and Precautions]

The following adverse reactions associated with the use of Lomustine Capsules were identified in clinical trials or postmarketingreports. Because these reactions were reported from a population of uncertain size, it is not possible to estimate their frequency, reliability, establishment a causal relationship to drug exposure.

Gastrointestinal disorders: nausea, vomiting, and stomatitis

Ocular disorders: optic atrophy, visual disturbances, and blindness

Neurologic disorders: disorientation, lethargy, ataxia, and dysarthria

Other: alopecia

OVERDOSAGE:
Overdosage with Lomustine Capsules has occurred, including fatal cases [see Dosage and Administration], Warnings and Precautions . Overdosage causes severe myelosuppression, as well as abdominal pain, diarrhea, vomiting, anorexia, lethargy, dizziness, abnormal hepatic function, cough, and shortness of breath.
No antidotes exist for Lomustine Capsules overdosage.

HOW SUPPLIED/STORAGE AND HANDLING:
How Supplied
Lomustine Capsules are available in four strengths and supplied as follows
LOMOOTHER 10 (Lomustine Capsules 10 mg) distinguishable by the color of the capsules, in individual bottle of 6 capsules each.
LOMOOTHER 40 (Lomustine Capsules 40 mg) distinguishable by the color of the capsules, in individual bottle of 6 capsules each.
LOMOOTHER 100 (Lomustine Capsules 100 mg) distinguishable by the color of the capsules, in individual bottle of 6 capsules each.

STORAGE AND HANDLING
Store at 25°C (77°F); excursions permitted to 15°C to 30°C (59°F to 86°F). Avoid temperatures over 40°C (104°F).
Lomustine Capsules is a cytotoxic drug. Follow applicable special handling and disposal procedures.
To minimize the risk of dermal exposure, always wear impervious gloves when handling bottles containing Lomustine Capsules. Do not break Lomustine Capsules; avoid exposure to broken capsules. If dermal contact occurs, wash areas of skin contact immediately and thoroughly.

REFERENCE LINK:
https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/017588s043lbl.pdf

MANUFACTURED BY
THERDOSE PHARMA PRIVATE LIMITED,
UNIT II, PLOT NO. 92A, ROAD NO. 8, ALEAP INDUSTRIAL ESTATE, PRAGATHI NAGAR, GAJULARAMARAM (V), MEDCHAL DISTRICT, TELANGANA STATE, INDIA.
Tel: + 91 – 40-65161624, www.therdose.com

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

OFFERTA ECONOMICA CEENU CPS 40 MG

Commerciale 2 <commerciale2@finternazionale.it>

mer 28/02/2024 14:20

A:Beni e Servizi <benieservizi@scamilloforlanini.rm.it>;

3 allegati (856 KB)

OFFERTA ECONOMICA CEENU.pdf; DICHIARAZIONE RESPONSABILITA' CEENU CPS 40 MG. BMS CANADA.pdf; CEENU - CANADA.pdf;

Gentilissimo Dott. Farfusola,
in allegato la nostra migliore offerta per il farmaco in oggetto.

Cordialmente

SI PRECISA CHE, DATA L'ATTUALE SITUAZIONE DI EMERGENZA SANITARIA A LIVELLO INTERNAZIONALE, POTREBBERO VERIFICARSI DEI RITARDI E/O BLOCCHI DEI TRASPORTI INTERNAZIONALI CON CONSEGUENTI RITARDI E/O BLOCCHI NELLE CONSEGNE DEI FARMACI.

FARMACEUTICA INTERNAZIONALE ITALIANA S.r.l. SI AVVALE SOLO ED ESCLUSIVAMENTE DI GROSSISTI E/O DITTE PRODUTTRICI CON REGOLARE AUTORIZZAZIONE ALLA VENDITA E/O PRODUZIONE DEI FARMACI RICHIESTI.
SI SPECIFICA CHE TALI CARATTERISTICHE SI EVINCONO DA DOCUMENTAZIONE UFFICIALE RICHIESTA AGLI ORGANI COMPETENTI DI CONTROLLO.

FARMACEUTICA INTERNAZIONALE ITALIANA
Francesca Boccoli

Corso Marconi, 26
28883 – GRAVELLONA TOCE (ITALY)
Tel.0323/86.55.57
Fax: 0323/84.52.67
e-mail: commerciale2@finternazionale.it
pec: farminternaz@pec.it

FARMACEUTICA INTERNAZIONALE ITALIANA S.r.l.
Partita I.V.A. 02130320035
Corso Marconi, 26 – 28883 GRAVELLONA TOCE
Tel.0323/86.55.57 - 84.08.05 - Fax 0323/84.52.67 cell.339/13.67.875
e mail: info@tinternazionale.it

Oggetto : OFFERTA ECONOMICA

Alla c.a. del Dott. Farfusola

Gravellona Toce **28 febbraio 2024** Riferimento Cliente Num. 494 OSPEDALE SAN CAMILLO FORLANINI

Pos.	Nome commerciale	Principio attivo	LOTTO COD C.I.G.	Confezionamento e dosaggio	Ditta produttrice titolare AIC	Paese di origine	Quantità prevista per unità	Prezzo a Voi riservato per cpr. o f.la	Prezzo a Voi riservato per Confezione	Note
1 A	Ceenu	Lomustina		20 Cps. 40 mg.	Bristol Myers Squibb	Canada		12,9200	258,40	MINIMO D'ORDINE N. 4 CONFEZIONI - SPESE DI TRASPORTO GRATUITE - TEMPI DI CONSEGNA ca. 10/12 gg. LAVORATIVI
1 B	Ceenu	Lomustina		20 Cps. 40 mg.	Bristol Myers Squibb	Canada		12,9200	258,40	MINIMO D'ORDINE N. 2 CONFEZIONI - SPESE DI TRASPORTO EURO 70,00 - TEMPI DI CONSEGNA ca. 10/12 gg. LAVORATIVI

Spese di Imballaggio e trasporto: VEDI NOTE
Spese di sdoganamento: G R A T U I T E
I.V.A : 10%

I prezzi rimarranno invariati salvo aumenti particolarmente significativi disposti dalla casa madre.

A disposizione per qualsiasi chiarimento in merito, l'occasione ci è gradita per inviarVi i ns. migliori saluti.

Pagamento entro 90 gg. Dalla data emissione Fattura

FARMACEUTICA INTERNAZIONALE ITALIANA S.r.l.
UFFICIO OFFERTE
Daniela Ferroni

Allegato 10

MODELLO 10-1

AL MINISTERO DELLA SALUTE
USMAF-SASN.....
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:
LOMUSTINA .....

nome commerciale: CEENU .....

forma farmaceutica.... COMPRESSE 40 MG. .....

nella quantità di numero.....confezioni contenenti.....20 COMPRESSE.....di farmaco cadauna.

Prodotto dalla ditta.....BRISTOL MYERS SQUIBB.....(Specificare il nome dell'Azienda)

Precisa che tale farmaco è regolarmente registrato nel Paese di provenienza: CANADA .....

Per il trattamento di : .....

Tale farmaco è indispensabile per la cura del Sig. (solo iniziali o codice) .....

Affetto da .....

Dichiaro 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:
Temperatura (es. -20°C, da 2 a 8°C, < 25°, <30°, nessuna indicazione):.....AMBIENTE.....

Altro: .....

Luogo e data _____

_____

Timbro e firma leggibile del medico *

*obbligatori

PRODUCT MONOGRAPH

PrCeeNU*

(Lomustine-CCNU)

Capsules; 10, 40 and 100 mg

Antineoplastic Agent

Bristol-Myers Squibb Canada
Montreal, Canada, H4S 0A4

Date of Preparation:

4 July 1974

* TM of Bristol-Myers Squibb Company
used under license by Bristol-Myers Squibb Canada

Date of Revision:
February 17, 2016

Submission control no.: 188932

PRODUCT MONOGRAPH

NAME OF DRUG

CeeNU

(Lomustine - CCNU)

Capsules; 10, 40 and 100 mg

THERAPEUTIC CLASSIFICATION

Antineoplastic Agent

CAUTION: CeeNU (LOMUSTINE-CCNU) IS A POTENT DRUG AND SHOULD BE USED ONLY BY PHYSICIANS EXPERIENCED WITH CANCER CHEMOTHERAPEUTIC DRUGS (SEE WARNINGS AND PRECAUTIONS). BLOOD COUNTS AS WELL AS RENAL AND HEPATIC FUNCTION TESTS SHOULD BE TAKEN REGULARLY. DISCONTINUE THE DRUG IF ABNORMAL DEPRESSION OF BONE MARROW IS SEEN.

ACTION AND CLINICAL PHARMACOLOGY

It is generally agreed that CeeNU (lomustine-CCNU) acts as an alkylating agent but, as with other nitrosoureas, it may also inhibit several key enzymatic processes.

CeeNU may be given orally. Following oral administration of radioactive CeeNU at doses ranging from 30 mg/m^2 to 100 mg/m^2about half of the radioactivity given was excreted within 24 hours. The serum half-life of the drug and/or metabolites ranges from 16 hours to 2 days. Tissue levels are comparable to plasma levels at 15 minutes after intravenous administration.

Because of the high lipid solubility and the relative lack of ionization at a physiological pH, CeeNU crosses the blood-brain barrier quite effectively. Levels of radioactivity in the CSF are 50 percent or greater than those measured concurrently in plasma.

INDICATIONS AND CLINICAL USES

CeeNU (lomustine-CCNU) is indicated as palliative therapy in addition to surgery and radiotherapy or in combination therapy with other chemotherapeutic agents in the following:

1. Brain tumors - both primary and metastatic, in patients who have already received appropriate surgical and/or radiotherapeutic procedures.

2. Hodgkin's Disease – as a secondary therapy, alone or in combination with other active drugs.

Other Tumors – CeeNU has been used in combination with other therapeutic agents in lung cancer (squamous cell, anaplastic large cell, and adenocarcinoma), malignant melanoma and breast cancer (advanced disease) only after other conventional methods have failed.

CONTRAINDICATIONS

CeeNU (lomustine-CCNU) should not be given to individuals who have demonstrated a previous hypersensitivity to it. Also it is contraindicated in patients having severe leukopenia and/or thrombocytopenia.

WARNINGS

CeeNU (lomustine-CCNU) should be administered by individuals experienced in the use of antineoplastic therapy.
Delayed bone marrow suppression, notably thrombocytopenia and leukopenia, which may contribute to bleeding and overwhelming infections in an already compromised patient, is the most common and severe of the toxic effects of CeeNU.

Blood counts should be monitored weekly for at least 6 weeks after a dose (see ADVERSE REACTIONS). At the recommended dosage, courses of CeeNU should not be given more frequently than every 6 weeks.

The bone marrow toxicity of CeeNU is cumulative and therefore dosage adjustment must be considered on the basis of nadir blood counts from prior dose (see Dosage Adjustment Table under DOSAGE AND ADMINISTRATION).

Caution should be used in administering CeeNU to patients with decreased circulating platelets, leukocytes or erythrocytes (see DOSAGE AND ADMINISTRATION).

Pulmonary toxicity including pulmonary infiltration and fibrosis (often fatal) from CeeNU appears to be dose related (see ADVERSE REACTIONS).

Liver and renal function tests should be monitored periodically (see ADVERSE REACTIONS).

Concomitant use of CeeNU with a live virus vaccine may potentiate the replication of the vaccine virus and/or may increase the adverse reaction of the vaccine virus because normal defense mechanisms may be suppressed by CeeNU. Vaccination with a live vaccine in a patient taking CeeNU may result in severe infection. Patient's antibody response to vaccines may be decreased. The use of live vaccines should be avoided and individual specialist advice sought (see PRECAUTIONS, Drug Interactions).

Carcinogenesis, Mutagenesis, Impairment of Fertility

CeeNU is carcinogenic in rats and mice, producing a marked increase in tumour incidence in doses approximating those employed clinically.

Nitrosourea therapy does have carcinogenic potential. Long-term use of nitrosoureas has been reported to be possibly associated with the development of secondary malignancies. The occurrence of acute leukemia and bone marrow dysplasias has been reported in patients following nitrosourea therapy.

CeeNU can have a mutagenic effect. Men treated with CeeNU are therefore advised not to father children during treatment and for up to 6 months afterwards, and to seek advice regarding sperm conservation before the start of treatment given the possibility of irreversible infertility caused by CeeNU therapy. CeeNU also affects fertility in male rats at doses somewhat higher than the human dose.

Pregnancy

Safe use in pregnancy has not been established. CeeNU is embryotoxic and teratogenic in rats and embryotoxic in rabbits at dose levels equivalent to the human dose. If this drug is used during pregnancy, or if the patient becomes pregnant while taking (receiving) this drug, the patients should be apprised of the potential hazard to the fetus. Women of childbearing potential should be advised to avoid becoming pregnant.

Nursing Mothers

Due to the lipophilic nature of CeeNU, it is likely to be excreted in breast milk. As a risk to the nursing child exists, a decision should be made whether to discontinue breastfeeding or to discontinue CeeNU therapy.

PRECAUTIONS

Due to delayed bone marrow suppression, blood counts should be monitored weekly for at least six weeks after a dose.

Baseline pulmonary function studies should be conducted along with frequent pulmonary function tests during treatment. Patients with a baseline below 70% of the predicted Forced Vital Capacity (FVC) or Carbon Monoxide Diffusing Capacity (DL_{co}) are particularly at risk.

Since CeeNU (lomustine-CCNU) may cause liver dysfunction, it is recommended that liver function tests be monitored periodically.

Renal function tests should also be monitored periodically.

Effects on ability to drive and to use machines

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

Drug Interactions

No drug interaction studies have been performed. It is unknown which hepatic enzymes are involved in lomustine-CCNU metabolism in humans. Animal studies suggest that CYP2C19, CYP2D6 and CYP3A4 are involved.

Drug-drug interactions of CeeNU with anti-epileptic drugs

Co-administration of some antiepileptic drugs and CeeNU can lead to complications secondary to pharmacokinetic interactions between the drugs.

Co-administration of enzyme-inducing antiepileptic drugs (e.g., carbamazepine, and phenytoin) may result in decreased blood concentration and reduced efficacy of CeeNU. Concurrent use of CeeNU with enzyme-inducing antiepileptic drugs should be avoided.

Co-administration of valproic acid or other enzyme-inhibiting drugs may impair the metabolism and increase the toxicity of CeeNU. Caution should be exercised when valproic acid and CeeNU are co-administered.

The toxic effects of valproic acid may be increased when combined with CeeNU.

Co-administration of CeeNU with phenytoin may lead to a decrease of phenytoin levels and a decrease in seizure control.

Other Interactions

There is increased risk of fatal systemic vaccine disease with the concomitant use of live vaccines. Live vaccines are not recommended in immunosuppressed patients including patients treated with CeeNU (see WARNINGS).

ADVERSE REACTIONS

1. Gastrointestinal: Nausea and vomiting may occur 3 to 6 hours after an oral dose and usually lasts less than 24 hours. The frequency and duration may be reduced by the use of antiemetics prior to dosing and by the administration of CeeNU (lomustine-CCNU) to fasting patients.

2. Hematologic Toxicity: The most frequent and most serious toxicity of CeeNU is delayed myelosuppression. It usually occurs four to six weeks after drug administration and is dose related. Thrombocytopenia occurs at about four weeks post-administration and persists for one to two weeks. Leukopenia occurs at five to six weeks after a dose of CeeNU and persists for one to two weeks.

   Approximately 65% of patients receiving 130 mg/m^2 develop white blood counts below 5000 $/mm^3$. Thirty-six percent developed white blood cell counts below 3000 $/mm^3$. Thrombocytopenia is generally more severe than leukopenia. However, both may be dose-limiting toxicities.

CeeNU may produce cumulative myelosuppression, manifested by more depressed indices or longer duration of suppression after repeated doses.

The occurrence of acute leukemia and bone marrow dysplasias have been reported in patients following long term nitrosourea therapy. Anemia also occurs, but is less frequent and less severe than thrombocytopenia or leukopenia.

3. Pulmonary Toxicity: Pulmonary toxicity characterized by pulmonary infiltrates and/or fibrosis has been reported rarely with CeeNU. Onset of toxicity has occurred after an interval of six months or longer from the start of therapy with cumulative doses of CeeNU usually greater than 1100 mg/m^2. There is one report of pulmonary toxicity at a cumulative dose of only 600 mg.

   Over a 25 years follow-up time of 17 childhood / adolescent cancer survivors of intracranial tumors treated with a related nitrosourea, 2 (12%) died of early onset pulmonary fibrosis (between 0-3 years post treatment) and 7 (41%) died of late onset pulmonary fibrosis (between 6 and 25 years post treatment). Of the remaining eight patients, seven had radiologic and physiologic (*i.e.*, lung function) evidence of upper zone pulmonary fibrosis. Patients treated at younger age seemed to be at greater risk of developing pulmonary fibrosis.

4. Other Toxicities: Stomatitis, alopecia, anemia have been reported infrequently.

   Neurological reactions such as disorientation, lethargy, ataxia and dysarthria have been noted in some patients receiving CeeNU. However, the relationship to medication in these patients is unclear.

5. Nephrotoxicity: Renal abnormalities consisting of decrease in kidney size, progressive azotemia and renal failure have been reported in patients who receive large cumulative doses after prolonged therapy with CeeNU and related nitrosoureas. Kidney damage has also been reported occasionally in patients receiving lower total doses.

6. Hepatotoxicity: A reversible type of hepatic toxicity, manifested by increased transaminase, alkaline phosphatase and bilirubin levels, has been reported in a small percentage of patients receiving CeeNU.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

For management of a suspected drug overdose, please contact your regional Poison Control Centre.

Accidental overdose with CeeNu (lomustine-CCNU) has been reported, including fatal cases. Accidental overdose has been associated with bone marrow suppression, abdominal pain, diarrhea, vomiting, anorexia, lethargy, dizziness, abnormal hepatic function, cough, and shortness of breath.

There is no specific antidote for overdose with CeeNU. In the case of overdosage, appropriate supportive measures should be taken.

Because of the lipophilic nature of the drug, the product is not dialyzable.

DOSAGE AND ADMINISTRATION

The recommended dose of CeeNU (lomustine-CCNU) is 130 mg/m^2 as a single dose by mouth every 6 weeks (see SPECIAL INSTRUCTIONS FOR USE, HANDLING AND DISPOSAL).

In individuals with compromised bone marrow function, the dose should be reduced to 100 mg/m^2 every 6 weeks.

A repeat course of CeeNU should not be given until circulating blood elements have returned to acceptable levels (platelets above 100,000/mm^3; leukocytes above 4,000/mm^3). Blood counts should be monitored weekly and repeat courses should not be given before 6 weeks because the hematologic toxicity is delayed and cumulative.

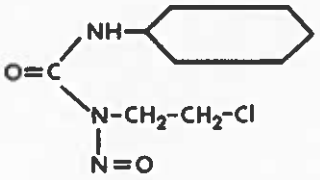
Doses subsequent to the initial dose should be adjusted according to the hematologic response of the patient to the preceding dose. The following schedule is suggested as a guide to dosage adjustment:

Nadir After Prior Dose		Percentage of Prior Dose to be Given
Leukocytes (/mm^3)	**Platelets (/mm^3)**	
≥4000	≥100,000	100%
3000 - 3999	75,000 - 99,999	100%
2000 - 2999	25,000 - 74,999	70%
< 2000	< 25,000	50%

When CeeNU is used in combination with myelosuppressive drugs, the doses should be adjusted accordingly.

PHARMACEUTICAL INFORMATION

Chemistry:



Trade Name: CeeNU

Proper Name: Lomustine

Chemical Name: 1-(2-chloroethyl)-3 cyclohexyl-1-nitrosourea

Molecular Formula: $C_9H_{16}ClN_3O_2$

Molecular Weight: 233.71

Description: Yellow powder. Soluble in 10% ethanol (0.05 mg/mL) and in absolute alcohol (70 mg per mL). It is relatively insoluble in water (<0.05 mg/mL). It is relatively un-ionized at a physiological pH.

STABILITY

Unopened bottles of CeeNU (lomustine-CCNU) capsules are stable for 36 months at room temperature.

Storage: PROTECT FROM LIGHT. Avoid excessive heat (over 40EC).

AVAILABILITY

The capsules of CeeNU (lomustine-CCNU) are prepared in three dosage strengths: 10 mg, 40 mg, and 100 mg.

All capsules contain mannitol and magnesium stearate as inert ingredients.

CeeNu capsules are available as follows:

- 10 mg in bottles of 20 capsules
- 40 mg in bottles of 20 capsules
- 100 mg in bottles of 20 capsules

SPECIAL INSTRUCTIONS FOR USE, HANDLING AND DISPOSAL

1. Only the appropriate number of CeeNU (lomustine-CCNU) capsules required for a single administration should be dispensed. Patients should be told that CeeNU is taken as a single oral dose and will not be repeated for at least 6 weeks.

2. Preparation of CeeNU should be done in a vertical laminar flow hood (Biological Safety Cabinet - class II)

3. CeeNU capsules should not be placed in automated counting machines. The counting and pouring of CeeNU should be done carefully and the equipment used should be rinsed with water and then thoroughly cleaned with detergent and water.

4. Personnel handling CeeNU should wear gloves, safety glasses, a mask and disposable protective clothing.

5. Vials and other materials which have come in contact with CeeNU should be segregated and incinerated at 1000EC or more. Sealed containers may explode. Intact vials should be returned to the manufacturer for destruction. Proper precautions should be taken in packaging these materials for transport.

6. Personnel regularly involved in the preparation and handling of CeeNU should have bi-annual blood examinations.

PHARMACOLOGY

The following is a summary of the data provided by the studies indicated in the attached list of references.

Kline et al used a biological procedure for the determination of drug levels of CeeNU (lomustine-CCNU). The biological target was L1210 leukemia. A dose response curve was determined for the drug when given simultaneously with the inoculation of a designated number of leukemia cells, using % of cures and median survival time as the parameters of response. The drug was also administered at a series of time intervals prior to the inoculation of leukemia cells and the dose level equivalence at the time of leukemic inoculation was estimated by reference of the observed therapeutic response to that obtained for the standard curve. The curve for percentage retention of administered CeeNU had a shallow slope and the half-life of the drug in the host was estimated to be 94 minutes.

Oliverio et al studied the metabolic fate of CeeNU using the ^{14}C label in each of three positions of the molecule; the ethyl, carbonyl, and cyclohexyl moieties. In rodents, 24 hours after intraperitoneal or oral dose of the ethyl or cyclohexyl labelled CeeNU, 75% of the radioactivity appeared in the urine, while about 10-20% of carbonyl or ethyl labelled CeeNU was expired as $^{14}CO_2$. In dogs and monkeys, CeeNU was also rapidly degraded and excretion of ^{14}C was primarily in the urine. Plasma levels of ^{14}C fell off rapidly in the first hour followed by a slower disappearance. After an intravenous injection, the CSF/plasma ratio of ethyl labelled CeeNU was three, while that for the cyclohexyl-labelled moiety was unity. This agrees with the observation that the cyclohexyl portion of the molecule is 60% plasma protein bound while the ethyl portion is not bound. The results support the suggested intermediate formation of an isocyanate moiety during the degradation of nitrosoureas *in vivo*. The identified metabolites and cyclohexylisocyanate were inactive against L-1210.

Studies conducted to determine the effects of NSC 79037 in polyethoxylated vegetable oil and normal saline (ratio of 1:9) applied topically to the hamster cheek pouch revealed no thromboembolism as concentrations 2.5 mg/ml. The only effect produced with this concentration was a slight decrease in the rate of venule and arteriole blood flow in 1/6 hamsters and a slight to moderate decrease in the venule flow of a second animal. Administration of a concentration at 0.625 mg/ml or the vehicle alone produced no detectable effect.

No thromboembolism was observed in the hamster cheek pouch microcirculation after single intrajugular injections of CeeNU in polyethoxylated vegetable oil and normal saline at doses ranging from 0.3125 to

20.0 mg/kg. However, a dosage of 0.625, 1.25, 2.5, 5.0, 10.0 or 20.0 mg/kg produced a decrease in cheek pouch venule blood flow varying from slight to moderate-severe. A slight to moderate-severe decrease in blood flow was also noted in the arterioles at drug levels ranging from 1.25 to 20 mg/kg with some vasoconstriction recorded at the 3 highest levels. At 20.0 mg/kg WBC stickiness was reported only once. The "no effect" level appeared to be 0.3125 mg/kg. Injection of the vehicle alone at volumes equivalent to those employed with 2.5, 5.0, 10.0, and 20.0 mg/kg drug dosages produced some vasoconstriction and a decrease in the rate of arteriole and venule blood flow. Microcirculation appeared normal when the vehicle alone was injected at a volume equivalent to that of a 1.25 mg/kg drug dosage. A mean recovery time of 17 minutes (5-35) was required for normal flow after intravenous injection in hamsters treated with the drug, compared to a mean recovery period of 6 minutes (2-10) in those receiving only the polyethoxylated vegetable oil and saline vehicle. It was concluded that cardiovascular effects observed were, in part, due to the vehicle employed.

Comparison of mortality levels in mice and rats for single oral doses of BiCNU and CeeNU on a mg/kg, mg/m^2, or mmole/kg basis revealed that BiCNU was twice as toxic as CeeNU.

TOXICOLOGY

The toxicity of CeeNU (lomustine-CCNU) was investigated primarily by the Mason Research Institute under contract with the National Cancer Institute. The parenteral toxicity of CeeNU may be summarized as follows:

a) Single Dose (IV infusion):

Dog:	Maximum tolerated dose (MTD) - 0.625 mg/kg
	Primary toxicity = Depressed hematopoiesis, lymphoid tissue.
	Secondary toxicity - Delayed hepatotoxicity
Rhesus Monkey:	MTD = 1.25 mg/kg
	Primary toxicity = nephrotoxicity
	Secondary toxicity - Depressed hematopoiesis, hepatotoxicity.

b) Multiple Dose (IV infusion):

Dog:	2 or 3 doses of 1.25 mg/kg given at weekly intervals = cumulative hepatotoxicity.

The toxicity of CeeNU given orally may be summarized as follows:

a) Single Dose (capsules)

Dog:	MTD = 2.0 mg/kg

b) Multiple Dose (capsules - dog, gavage - monkey)

Dog:	MTD - 0.65 mg/kg/day x 14
Rhesus Monkey:	MTD = 0.15 mg/kg/day x 14

c) Delayed Hepatotoxicity (capsules)

Dog:	A single oral dose of 4 mg/kg produced hepatotoxicity that persisted for 2-3 months after drug treatment.

REFERENCES

1. Hansen, H., Selawry, O., Muggia, F.M. and Walker, M.D.
Clinical studies with 1(2-chloroethyl)-3-cyclohexyl-1-nitrosourea (NSC 79037)
Cancer Research Vol. 31: 223-227, 1971.

2. Israel, L. and Chahinian, P.
Comparative Toxicity on Leukocyte and Platelet of Two Regimens of CCNU.
E.O.R.T.C. Report.

3. Israel, L., et al.
Analysis of Growth Curve Modifications in 30 Measurable Tumors, Under the Influence of 75 mg/M2 of CCNU Every 3 Weeks.
E.O.R.T.C. Report.

4. Protocol ALB #7282. Methyl-CCNU and CCNU in the Treatment of Advanced Malignant Solid Tumors of Adults.
Acute Leukemia Group B Report. August 1973.

5. CCNU Phase II Study Report. COG 7120. Central Oncology Group Report. August 1973.

6. WCG 809. CCNU (NSC-79037) Given Orally for the Treatment of Lymphoma and other Neoplasma. A Phase II Study.
Western Cooperative Group Report. June 1973.

7. Hoogstraten, B., Gottlieb, J., Caoli, E., Tucker, W., Talley, R. and Haut, A.
CCNU (1-[2-chloroethyl]-3-cyclohexyl-1-nitrosourea, NSC-79037) in the Treatment of Cancer.
Cancer Vol. 32: 38-43, 1973.

7A. Hoogstraten, B., and Luce, J.
CCNU (1-[2-chloroethyl]-3-cyclohexyl-1-nitrosourea) and Bleomycin in the Treatment of Solid Tumors and Lymphoma.
Proc. of the Amer. Assoc. for Cancer Research, Abstracts No. 9, March 1973

8. DeConti, R., Hubbard, S., Pinch, P. and Bertino, J.
Treatment of Advanced Neoplastic Disease with 1-[2-chloroethyl]-3-cyclohexyl-1-nitrosourea (CCNU; NSC-79037).
Cancer Chemotherapy Reports Vol. 57: 201-207, 1973.

9. Broder, L. and Hansen, H.
1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea (CCNU, NSC-79037): A Comparison of Drug Administration at Four-week and Six-week Intervals.
European Journal of Cancer Vol. 9: 147-152, 1973.

10. Perloff, M., Muggia, F., and Ackerman, C.
Role of a Nitrosourea (Lomustine) in Advanced Non-hematologic Cancer: Clinical Experience and Review. Unpublished Report.

11. Bertolone, S., Holton, C., Pratt, C. and Short, B.
Response of Advanced Childhood Malignancy to 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea (CCNU).
Western Pediatric Hematology Abstract.

12. Fewer, D., Wilson, C., Boldrey, E. and Enot, J.
Phase II Study of 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea (CCNU; NSC-79037) in the Treatment of Brain Tumors.
Cancer Chemotherapy Reports Vol. 56: 421-427, 1972.

12A. Rosenblum, M., Reynolds, A., Smith, K., Rumack, B. and Walker, M.
Chloroethyl-cyclohexyl-nitrosourea (CCNU) in the Treatment of Malignant Brain Tumors.
Journal of Neurosurgery Vol. 39: 306-314, 1973.

13. Hansen, H., and Muggia, F.
Treatment of Malignant Brain Tumors with Nitrosoureas (Letter).
Cancer Chemotherapy Reports Vol. 55: 99-100, 1971.

14. Gottlieb, J.A., Bonnet, J., Hoogstraten, B. and O'Bryan, R.
Superiority of Adriamycin over Oral Nitrosoureas in Patients with Breast Cancer. Report on SWG-449
Southwest Cancer Chemotherapy Study Group.

15. Krakoff, I.
Summary of Adriamycin/CCNU Comparison in Patients with Breast Cancer. Unpublished Report.

16. Ahmann, D., Bisel, H. and Hahn, R.
Difficulties Designing Clinical Trials as Exemplified by a Phase 2 Drug Evaluation of 5[3,3-Bis(2-chloroethyl)-1-triazenol]-indazole-4-carboxamide and 1-(2-Chloroethyl)-3-cyclohexyl-1-nitrosourea in Patients with Disseminated Breast Cancer.
Cancer Research Vol. 33: 1707-1710, 1973.

17. Cunningham, T.J., Rosner, D., Olson, K.B., Nemoto, T., Dao, T., and Horton, J.
A Comparison of 5 Azacytidine (5AC) with CCNU in Breast Cancer.
Proc. of the Amer. Assoc. for Cancer Research. Abstract 356, 1973.

18. EST 0571. Master Protocol for the Evaluation of New Treatments in Patients with Metastatic Breast Carcinoma (Phase II).
Eastern Cooperative Oncology Group Report.

19. Moertel, C.
Treatment of Advanced Gastrointestinal Cancer with the Nitrosoureas. Unpublished Report (New Drug Liason Meeting-National Cancer Institute, February 1973).

20. Moertel, C., Schutt, A., Reitemeier, R and Hahn, R.
Sequential 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea (NSC 79037) and 5-Fluorouracil (NSC 19893) Therapy of Gastrointestinal Cancer.
Cancer Research Vol. 32: 1280-1282, 1972.

20A. Moertel, C., Schutt, A., Reitemeier, R. and Hahn, R.
A Phase II Study of 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea (NSC 79037) in the Palliative Management of Advanced Gastrointestinal Cancer.
Cancer Research Vol. 32: 1278-1279, 1972.

21. Moertel, C., Reitemeier, R., Schutt, A., and Hahn, R.
Effect of Resection of the Primary Neoplasm on Responsiveness to Chemotherapy of Patients with Large Bowel Cancer.
Cancer Chemotherapy Reports Vol. 56: 551-552, 1972.

22. Klassen, D. and Rapp, E.
Phase II Study of CCNU in the Treatment of Advanced Gastrointestinal Malignancy. Abstract 90
Cancer Chemotherapy Reports, 1973.

23. EST 0870. Protocol for the Continuous Evaluation of New Treatments in Patients with Metastatic Carcinoma of the Colon and Rectum. Eastern Cooperative Oncology Group Protocol.

24. Selawry, O., and Hansen, H.
Superiority of CCNU (1-(2-Chloroethyl)-3-cyclohexyl-1-nitrosourea; NSC 79037) over BCNU (1,3-bis (2-chloroethyl)-1-nitrosourea; NSC 409962) in Treatment of Advanced Hodgkin's Disease. Abstract 182
Proc. of the Amer. Assoc. for Cancer Research, and Acute Leukemia Group B Protocol 6753 Report.

25. Takita, H. and Brugarolas, A.
Effect of CCNU (NSC-70837) on Bronchogenic Carcinoma.
Journal of the Nat. Cancer Inst. Vol. 50: 49-53, 1973.

26. Carr, D.
Lung Cancer. CCNU/Methyl CCNU.
Unpublished Report, June 1973.

27. Veternans Administration Lung Cancer Study Report. Report of April 1972.

28. Ahmann, D., Hahn, R. and Bisel, H.
A Comparative Study of 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea (NSC 79037) and Imidazole Carboxamide (NSC 45388) with vincristine (NSC 67574) in the Palliation of Disseminated Malignant Melanoma.
Cancer Research Vol. 32: 2432-2434, 1972.

29. WCG 119. CCNU versus CCNU + Vincristine for Treatment of Disseminated Malignant Melanoma. Phase III - Randomized.
Western Cancer Group Report.

30. Mittelman, A., David, A., and Murphy, G.
Lomustine Treatment of Metastatic Renal Cell Carcinoma.
Journal of the Amer. Med. Assoc. Vol. 225: 32-35, 1973.

31. Mittelman, A., and Murphy, G.
Treatment of Metastatic Renal Cell Carcinoma with 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea (CCNU).
Abstract 115, 1972.

32. Costanza, M.
Eastern Cooperative Oncology Group Report.

33. Einhorn, L., Livingston, R. and Gottlieb, J.
Combination Chemotherapy with Adriamycin (NSC 123,127) and 1-(2-chloroethyl)-3 -cyclohexyl-1-nitrosourea (CCNU, NSC 79037).
Unpublished Report.

34. Wallace, H.J., Hoagland, H., Ellison, R., Glidewell, O., and Holland, J.
CCNU Plus Cytosine Arabinoside (ARA-C) Treatment of Acute Myelocytic Leukemia Compared with Thioguanine (TG) Plus ARA-C. Abstract 400
Proc. of the Amer. Assoc. for Cancer Research. Report on Protocol ALB 7121.

35. Protocol ALB 7121. Comparison of Intermittent ARA-C + TG with ARA-C + CCNU (Induction). Acute Leukemia Group B Report.

36. Protocol ALB 7132. Attempted Prevention of Blast Crisis in CML, by the Use of Pulsed Doses of CCNU and ARA-C. Acute Leukemia Group B Report.

37. EST 0671. Combination Chemotherapy for Metastatic Lung Cancer. Eastern Cooperative Oncology Group Report.

38. ALB 7251. A Study of 4 Drug Combination Chemotherapy of Stage III and IV Hodgkin's Disease. Acute Leukemia Group B Report.

39. WCG-120. COP versus CCNU-OP in Non-Hodgkin's Lymphoma.
Western Cooperative Group Report.

40. Magrath, I. and Ziegler, J.
Prophylaxis of Meningeal Burkitt's Lymphoma with CCNU. Abstract 265, March 1973.

41. Ziegler, J.
Chemotherapy of Burkitt's Lymphoma.
Cancer 30: 1534-1540, 1972.

42. Carter, R. and Krementz, E.
Combination Treatment of Metastatic Malignant Melanoma with Urea, 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea (CCNU), Vincristine (VCR) and Dimethyltriazeno Imidazole Carboxamide (DIC). Abstract 351
Proc. of the Amer. Assoc. for Cancer Research. 1971.

43. COG 7130. DTIC and Combination Therapies for Metastatic Melanoma. Phase III. Central Oncology Group Report.

44. Gerner, R.
Unpublished Report from Roswell Park Memorial Institute.

45. CCNU Pilot Study. Acute Leukemia Group B. Report.

46. Harley, J., Ramanan, S., Monta, L., Valentine, M., and Gustke, S.
The Cyclic Use of CCNU, Cytoxan and Alkeran Plus Prednisone in Patients with Multiple Myeloma.
Unpublished Report.

47. Lindell, T., Moseley, H., and Fletcher, W.
Combination CCNU-Bleomycin Therapy for Squamous Cell Carcinoma.
Central Oncology Group Report.

48. Fletcher, W.
4-Drug Combination Therapy for Squamous Cell Carcinoma Using CCNU, Methotrexate, Velban and Bleomycin.
Central Oncology Group Report.

49. Little, Arthur, D. Inc.
Effects of CCNU (NSC 79037) in polyethoxylated vegetable oil and normal saline on the micro-circulation of the hamster cheek pouch after topical application and intravenous injection.

50. Kline, Ira, et al.
Duration of Drug Levels in Mice as indicated by residual antileukemic efficacy Chemotherapy 13: 28-41, (1968).

51. Oliverio, Vincent, T. et al.
The absorption, distribution, excretion and biotransformation of the carcinostatic 1-(2-Chloroethyl)-3-cyclohexyl-1-nitrosourea in animals.
Cancer Research Vol. 30: 1330-1337, May 1970.

52. Thompson, George, R. and Larson, Robert E.
A Toxicologic comparison of the potency and activity of 1,3-Bis (2-chloroethyl)-1 -nitrosourea (BCNU) and 1-(2-Chloroethyl)-nitrosourea (CCNU) in mice and rats. Toxicology and applied Pharmacology Vol. 21: 405-413, (1972).

53. Dent, R.G.
Fatal pulmonary toxic effects of lomustine.
Thorax Vol. 37: 627-629, (1982).

54. Vats, Tribhawan, S. and Langston, Claire M.
Pulmonary fibrosis associated with lomustine (CCNU): A Case Report.
Cancer Treat. Rep. Vol. 66 (10): 1881-1882.

55. The Medical Letter 1976.

56. Cruz, A.B., Metter, G., Armstrong, D.M., Aust, J.B., Fletcher, W.S., Wilson, W.L., and Richardson, J.D.
Treatment of Advanced Malignancy with CCNU (NSC 79037). A Phase II Cooperative Study with Long-Term Follow-up.
Cancer Vol. 38: 1069-1076, 1976.

57. Silver, H.K.B. and Morton, D.L.
CCNU Nephrotoxicity Following Sustained Remission in Oat Cell Carcinoma. Cancer Treat. Rep. Vol. 63 (2): 226-227, 1978.

58. ASHP Technical Assistance Bulletin on Handling Cytotoxic and Hazardous Drugs.
Am. J. Hosp. Pharm. 1990; 47: 1033-1049.

59. OSHA Work-Practice Guidelines for Personnel Dealing with Cytotoxic (Antineoplastic) Drugs.
Am. J. Hosp. Pharm. 1986; 43: 1193-1204.

60. O'Driscoll, B.R. et al.
Active Lung Fibrosis Up to 17 Years After Chemotherapy With Carmustine (BCNU) In Childhood.
N. Engl. J. Med. 1990; 323: 378-382.

MONDIALPHARMASA

CORSO ELVEZIA, 16
CH – 6901 LUGANO
Tel. +41 91 / 682 42 40
Fax +41 91 / 682 07 81
info@mondialpharma.ch
VAT No. CHE – 152.434.145

U.O.C. Acquisizione Beni e Servizi
Ufficio Acquisizione Farmaci e Diagnostici
Tel.06 58706762- 6733-4554
E-mail: benieservizi@scamilloforlanini.rm.it

Spett.le AZ. OSP. S. CAMILLO-FORLANINI
Dott. Farfusola
Roma

27.02.2024

OFFERTA ANNUALE PER FARMACI ESTERI :2024

Abbiamo il piacere di sottoporVi l'offerta dei seguenti medicinali Esteri non registrati o carenti in Italia.

VS.RIF fax/email/tel PROT N° 0007777/2024 del : 27/02/2024

– *Nome – commerciale* –	*Prezzo per Confezione Euro*	*Prezzo Unitario Euro*	*Casa Produttrice* ----------
BELUSTINE 40 mg X 10 cpr ***Lomustine –*** ***Disponibile in magazzino***	***16,0000***	***1,6000***	**MEDICLONE BIOTECH** ***INDIA***

**** Condizioni di vendita:***
**** Prezzi : Netti Ospedale più Iva al 10% a parte in fattura in Euro, ed eventuale trasporto.***
****. Costo spedizione :***
a) le spese di trasporto: 26.00Euro - Sono GRATUITE Per ordini superiori ad Euro 400.00
b) le spese di sdoganamento: Euro 14.00 + IVA 10%. Per ogni spedizione.
DOGANA CASELLE (TORINO)
c) si alleghera' modulo Autor. Sanitaria e sarà ns. competenza espletare tutte le pratiche,in merito, per l'invio a Vs. destinazione di quanto ordinato.
1) Termini di consegna: 8/12. gg. lavorativi , Urgenze: 4/5 gg. lav. se già in ns. magazzino.
2) Termini di pagamento: Bonifico Bancario 60.gg. data fattura.
3) Validità dei prezzi: ANNO 2023 *SALVO aumenti disposti dalle "Case Produttrici - distributori"

Nel frattempo ,porgiamo, distinti saluti.
MONDIAL PHARMA SA

Mondial Pharma S.A.
Via D. Alighieri - C.P. 1624
6830 CHIASSO (Switzerland)
Tel. +41/ 91 682 42 40 Fax +41/ 91 682 07 81
info@mondialpharma.ch

SISTEMA SANITARIO REGIONALE
AZIENDA OSPEDALIERA
SAN CAMILLO FORLANINI

REGIONE LAZIO

U.O.C. Programmazione Strategica e Controllo di Gestione

“

Allegato “Autorizzazione di spesa”

Proposta di delibera 444/2024

Anno	Aut. di spesa N°	Sub N°	Mod N°	Conto	Budget (disponibilità assegnata)	Totale sub-autorizzato (utilizzato)	Importo attuale	Residuo disponibile
2024	**3**	**142**		**501010113000**	**16 447,00**	**12 243,00**	**46,97**	**4 157,03**
2024	**3**	**143**		**502020107000**	**904,00**	**251,40**	**36,90**	**615,70**
	TOTALE PRESENTE AUTORIZZAZIONE **€ :**							

Anno	Aut. di spesa N°	Sub N°	Mod N°	Conto	Importo pluriennale	Totale sub-autorizzato		

Conto Economico/Patrimoniale	DESCRIZIONE
501010113000	**MEDICINALI ESTERI - SENZA AIC**
502020107000	**SERVIZI TRASPORTI (NON SANITARI)**