Module 1.3.2 PATIENT INFORMATION LEAFLET

Line	PROPOSED PATIENT INFORMATION LEAFLET
1	**PATIENT INFORMATION LEAFLET**
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3	**SCHEDULING STATUS: S4**
4	
5	**DETENER 6 mg/ml concentrate for solution for infusion**
6	**Busulfan**
7	Sugar free
8	**Read all of this leaflet carefully before you are given DETENER**
9	• Keep this leaflet. You may need to read it again.
10	• If you have further questions, please ask your doctor, pharmacist,
11	nurse or other health care provider.
12	
13	
14	**What is in this leaflet**
15	1. What **DETENER** is and what it is used for
16	2. What you need to know before you are given **DETENER**
17	3. How to use **DETENER**
18	4. Possible side effects
19	5. How to store **DETENER**
20	6. Contents of the pack and other information
21	
22	**1. What DETENER is and what it is used for**
23	

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24 25 26 27 28 29 30 31 32	**2. DETENER** contains the active substance busulfan, which belongs to a group of medicines called alkylating medicines. **DETENER** destroys the original bone marrow before the transplant. **DETENER** is used in adults as a treatment prior to transplantation in combination with cyclophosphamide. You will receive this preparative medicine before receiving a transplant of either bone marrow or haematopoietic progenitor cell.
33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48	**2. What you need to know before you use DETENER** **DETENER should not be administered to you:** • if you are hypersensitive (allergic) to busulfan or any of the other ingredients of **DETENER** (listed in section 6) • if you are pregnant or breast feeding your baby • if you suffer from hepatic insufficiency **Warnings and precautions** Special care should be taken with **DETENER**: **DETENER** is a potent cytotoxic medicine that results in profound decrease of blood cells. At the recommended dose, this is the desired effect. Therefore, careful monitoring will be performed. You should tell your doctor: • if you have a liver, kidney, heart or lung problem

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49	• if you have a history of seizures
50	• if you are currently taking other medicines.
51	
52	Cases of formation of blood clots in the small blood vessels may appear
53	after hematopoietic cell transplantation (HCT) with high-dose of your
54	treatment in combination with other medicines.
55	
56	Acute respiratory distress syndrome (severe shortness of breath) has been
57	reported.
58	Busulfan can impair fertility.
59	
60	**Other medicines and DETENER**
61	Always tell your health care provider if you are taking any other medicine.
62	(This includes complementary or traditional medicines.)
63	
64	**DETENER** may interact with other medicines.
65	Particular caution should be taken if you use itraconazole (used to treat
66	fungal infections) and or ketobemidone (used to treat pain), because this may
67	increase the side-effects.
68	The use of paracetamol during the 72 hours prior to or with **DETENER**
69	administration should be used with caution.
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73	

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74	**Pregnancy, breastfeeding and fertility**
75	If you are pregnant or breastfeeding, think you may be pregnant or are
76	planning to have a baby, please consult your health care provider for advice
77	before you receive treatment with **DETENER.**
78	
79	Women must not be pregnant during treatment with **DETENER** and up to 6
80	months after treatment.
81	
82	**Breast-feeding**
83	Women must stop breast-feeding before starting their treatment with
84	**DETENER**.
85	
86	**Fertility**
87	It may no longer be possible for you to achieve a pregnancy (infertility) after
88	treatment with **DETENER**. If you are concerned about having children, you
89	should discuss this with your doctor before treatment.
90	
91	Adequate contraceptive precautions should be used when either partner is
92	receiving **DETENER**.
93	Men treated with **DETENER** are advised not to father child during and up to
	6 months after treatment.
94	**3. How to use DETENER**
95	You will not be expected to give yourself **DETENER**. It will be given to you by
96	a health care provider who is qualified to do so**.**

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97 98 99 100 101 102 103 104 105 106 107 108 109 110 111 112 113 114 115 116	The dose will be calculated according to your body weight. The recommended dose is 0,8 mg/kg of body weight in adult patients in combination with cyclophosphamide. **Medicines before you receive DETENER:** - anticonvulsive medicines to prevent seizures - antiemetic medicines to prevent vomiting **Route of administration** **DETENER** is administered by a qualified health care professional as a central intravenous infusion, after dilution of the individual ampoule. Each infusion will last 2 hours. **DETENER** will be administered every 6 hours during 4 consecutive days prior to transplant. **If you take more DETENER than you should** Since a health care provider will administer **DETENER**, he/she will control the dosage. However, in the unlikely event of overdosage your doctor will manage the overdosage.
117 118 119 120 121	**4. Possible side effects** **DETENER** can have side effects.

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122	Not all side effects reported for **DETENER** are included in this leaflet. Should
123	your general health worsen or if you experience any untoward effects while
124	taking **DETENER**, please consult your health care provider for advice.
125	
126	If any of the following happens, you will have to stop taking **DETENER**:
127	• swelling of the hands, feet, ankles, face, lips and mouth or throat, which
128	may cause difficulty in swallowing or breathing',
129	• 'rash or itching',
130	• 'fainting'
131	
132	These are all very serious side effects. If you have them, you may have had a
133	serious reaction to **DETENER**. You may need urgent medical attention or
134	hospitalisation.
135	
136	Tell your doctor immediately or go to the casualty department at your nearest
137	hospital if you notice any of the following:
138	• decrease in circulating blood cell counts as shown by the blood tests
139	(intended effect of the drug to prepare you for your transplant infusion).
140	• infection, liver disorders including blocking of a liver vein, graft versus
141	host disease (the graft attacks your body) and lung complications.
142	Your doctor will monitor your blood counts and liver enzymes regularly to
143	detect and manage these events.
144	
145	These are all serious side effects. You may need urgent medical attention.
146	

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147	Tell your doctor if you notice any of the following:
148	<u>Frequent side effects:</u>
149	• decrease of blood circulating cells (red and white) and platelets,
150	• insomnia,
151	• anxiety,
152	• dizziness,
153	• depression,
154	• confusion
155	• decrease in magnesium, calcium, potassium phosphate and sodium in
156	blood
157	• increase in blood sugar,
158	• increase in heart rate,
159	• increase or decrease of blood pressure,
160	• vasodilation,
161	• blood clots,
162	• changes and abnormalities in heart rhythm,
163	• fluid retention or inflammation around the heart,
164	• decreased heart output,
165	• shortness of breath,
166	• nasal secretion,
167	• sore throat,
168	• cough,
169	• hiccup,
170	• nosebleeds,
171	• abnormal breath sounds,

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172	• increase in breath rhythm,
173	• respiratory failure,
174	• alveolar bleeding,
175	• asthma,
176	• collapse of small portions the lung,
177	• fluid around the lung,
178	• nausea,
179	• inflammation of the mucosa of the mouth,
180	• vomiting,
181	• loss of appetite,
182	• diarrhoea,
183	• constipation,
184	• heart burn,
185	• anus discomfort,
186	• inflammation of the mucosa of oesophagus,
187	• paralysis of the gut,
188	• vomiting blood.
189	• jaundice,
190	• elevate liver enzymes,
191	• enlarged liver,
192	• rash,
193	• itching,
194	• loss of hairs,
195	• back, muscle and joint pain,
196	• increase in creatinine elimination,

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197	• discomfort in urination and decrease in urine output,
198	• increase in amounts of nitrogen in the blood stream,
199	• blood in the urine,
200	• moderate renal insufficiency,
201	• weight increase,
202	• fever,
203	• headache,
204	• abdominal pain,
205	• weakness,
206	• chills,
207	• pain,
208	• oedema,
209	• general pain and inflammation at the injection site,
210	• chest pain
211	
212	• <u>Less frequent side effects:</u>
213	• delirium,
214	• nervousness,
215	• hallucination,
216	• agitation,
217	• abnormal brain function,
218	• cerebral haemorrhage
219	• seizure,
220	• clotting of femoral artery,
221	• thrombosis,

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222	• extra heart beats,
223	• decrease in heart rate,
224	• diffuse leak of fluid from the capillaries (small blood vessels),
225	• decrease in blood oxygen,
226	• bleeding in the stomach or gut.
227	
228	If you notice any side effects not mentioned in this leaflet, please inform your
229	doctor or pharmacist.
230	
231	**Reporting of side effects**
232	If you get side effects, talk to your doctor, pharmacist or nurse. You can also
233	report side effects to SAHPRA via the "**6.04 Adverse Drug Reaction**
234	**Reporting Form**", found online under SAHPRA's publications:
235	https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you
236	can help provide more information on the safety of **DETENER.**
237	
238	**5. How to store DETENER**
239	Store all medicines out of reach of children. Do not freeze.
240	
241	*Unopened vials:*
242	Store in a refrigerator between 2 ^{o}C to 8 ^{o}C. Excursions not permitted.
243	
244	*Chemical and physical in-use stability after dilution:*
245	8 hours (including infusion time) after dilution in glucose 5% or sodium
246	chloride 9 mg/ml (0.9%) solution for injection when stored at 20 °C ± 5 °C.

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248	6 hours after dilution in sodium chloride 9 mg/ml (0.9%) solution for injection
249	when stored at 2 °C-8 °C followed by 3 hours stored at 20 °C ± 5 °C
250	(including infusion time).
251	
252	**6. Contents of the pack and other information**
253	**What DETENER contains**
254	Each 1 ml of concentrate contains 6 mg of busulfan (60 mg in 10 ml).
255	After dilution: Each 1 ml of solution contains 0.5 mg of busulfan.
256	The other ingredients are citric acid anhydrous, macrogol 400 and purified N,
257	N-dimethyl acetamide.
258	
259	**What DETENER looks like and contents of the pack**
260	Clear, colourless solution free from visible particles.
261	
262	Busulfan 6mg/ml concentrate for solution for infusion is packed in 11 ml clear
263	tubular Lyo Type I glass vial with a 20mm purple flip off aluminium seal and a
264	20mm rubber stopper. The vials are packaged into folded cardboard cartons
265	with a leaflet enclosed.
266	Busulfan is packed in a single pack of 1 vial and 8 single cartons are packed
267	in a shrink sleeve.
268	
269	**Holder of Certificate of Registration**
270	Emcure Pharmaceuticals SA (Pty) Ltd.
271	Arizona House, First floor, South Wing, Aspen Business Park

Line	PROPOSED PATIENT INFORMATION LEAFLET
272	1 Madison Avenue, Aspen Lakes, Extension 13
273	Johannesburg South,
274	2190
275	
276	**This leaflet was last revised in**
277	Not applicable
278	
279	**Registration number**
280	56/26/0353