3 March 2015
EMA/COMP/256/2004 Rev.3
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Dexrazoxane for the treatment of anthracycline extravasation

First publication	15 June 2009
Rev.1: transfer of sponsorship	3 March 2011
Rev.2: transfer of sponsorship	4 October 2013
Rev.3: transfer of sponsorship	3 March 2015
Disclaimer Please note that revisions to the Public Summary of Opinion are purely administrative updates. Therefore, the scientific content of the document reflects the outcome of the Committee for Orphan Medicinal Products (COMP) at the time of designation and is not updated after first publication.	

On 19 September 2001, orphan designation (EU/3/01/059) was granted by the European Commission to TopoTarget A/S, Denmark, for dexrazoxane for the treatment of anthracycline extravasation.

The sponsorship was transferred to SpePharm Holding B.V., The Netherlands, in September 2010 and subsequently to Norgine B.V.,The Netherlands, in September 2013. In July 2014 the sponsorship was transferred to Clinigen Healthcare Ltd., United Kingdom.

What is anthracycline extravasation?

Chemotherapeutic agents (medications that are used to treat various forms of cancers) are mostly given by intravenous administration. When given intravenously, there are few side effects at the site of injection. However, when injected or leaked outside the vein into the surrounding tissues, defined as extravasation, a tissue reaction spanning from irritation to necrosis (cell death) may arise. In particular, anthracycline (a chemotherapeutic agent) leaked outside the vein is continuously released from necrotic (dead) cells in the surrounding tissues and causes damage to adjacent healthy tissue. This leads to severe tissue damage and deep ulcerations (skin lesions) that progress slowly over several weeks. Anthracycline extravasation is chronically debilitating.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

What is the estimated number of patients affected by the condition?

At the time of designation, anthracycline extravasation affected approximately 0.03 in 10,000 people in the European Union (EU). This was equivalent to a total of around 1,100 people*, and is below the threshold for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and the knowledge of the Committee for Orphan Medicinal Products (COMP).

What treatments are available?

At the time of submission of application for orphan drug designation there were no authorised products for the treatment of anthracycline extravasation in the European Union. However, several methods were used to prevent and treat anthracycline extravasation, such as elevation of the affected limb or cooling. In some cases dimethyl sulfoxide, hyberbaric oxygen or surgical intervention were used.

How is this medicine expected to work?

Dexrazoxane is structurally similar to ethylenediaminetetraacetic acid, a chelating agent (an agent that binds metal ions). It is believed to bind iron and conceal it from oxygen. Anthracycline induces the formation of free radicals (active molecular fragment containing a chemical charge) leading to breaks in the DNA (the genetic material in the cell). Although the mechanism of action of dexrazoxane in anthracycline extravastion is not completely understood, it is believed to inhibit formation of DNA breaks by scavenging iron and preventing free radical formation. These effects are expected to protect against the toxic damages of tissues and cells caused by anthracyclines.

What is the stage of development of this medicine?

The effects of dexrazoxane were evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials in patients with anthracycline extravasation were initiated.

Dexrazoxane was not marketed anywhere worldwide for treatment of anthracycline extravasation, at the time of submission.

Orphan designation of dexrazoxane was granted in the United States for treatment of anthracycline extravasation during chemotherapy in 2004. Dexrazoxane has been authorised in the United States for the treatment of extravasation resulting from IV anthracycline chemotherapy since 2007.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 18 July 2001 recommending the granting of this designation.

Update: Dexrazoxane (Savene) has been authorised in the EU since 28 July 2006 for for the treatment of anthracycline extravasation.

More information on Savene can be found in the European public assessment report (EPAR) on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports

*Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed on the basis of data from the European Union.
At the time of designation, this represented a population of 378,800,000 (Eurostat 2001).

Opinions on orphan medicinal product designations are based on the following three criteria:

- the seriousness of the condition;
- the existence of alternative methods of diagnosis, prevention or treatment;
- either the rarity of the condition (affecting not more than 5 in 10,000 people in the EU) or insufficient returns on investment.

Designated orphan medicinal products are products that are still under investigation and are considered for orphan designation on the basis of potential activity. An orphan designation is not a marketing authorisation. As a consequence, demonstration of quality, safety and efficacy is necessary before a product can be granted a marketing authorisation.

For more information

Sponsor's contact details:

Clinigen Healthcare Ltd.
Pitcairn House
Crown Square
First Avenue
Burton-on-Trent
Staffordshire DE14 2WW
United Kingdom
Tel. +44 (0)7714 135 765
Fax +44 (0)1283 494 341
http://www.clinigengroup.com/patients

For contact details of patients' organisations whose activities are targeted at rare diseases see:

- Orphanet, a database containing information on rare diseases which includes a directory of patients' organisations registered in Europe.
- European Organisation for Rare Diseases (EURORDIS), a non-governmental alliance of patient organisations and individuals active in the field of rare diseases.

Translations of the active ingredient and indication in all official EU languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Dexrazoxane	Treatment of anthracycline extravasations
Bulgarian	Декстразоксан	Лечение на антрациклинови екстравазации
Croatian	Deksrazoksan	Liječenje ekstravazacije antraciklina
Czech	Dexrazoxan	Léčba antracyklinové extravazace
Danish	Dexrazoxan	Behandling af extravasationer efter anthracykliner
Dutch	Dexrazoxan	Behandeling van anthracyclinen extravasatie
Estonian	Deksrazoksaan	Antratsükliini ekstravasatsiooni ravi
Finnish	Deksratsoksaani	Antrasykliinien ekstravasaation hoito
French	Dexrazoxane	Traitement des extravasations d´anthracyclines
German	Dexrazoxan	Behandlung von Extravasationen von Anthracyklinen
Greek	Ντεξραζοξάνη	Θεραπεία της εξωαγγειακής διαρροής ανθρακυκλινών
Hungarian	Dexrazoxan	Anthracyclin extravazáció kezelésére
Italian	Dexrazoxane	Trattamento dello stravaso di antracicline
Latvian	Deksrazoksāns	Antraciklīna ekstravazācijas ārstēšana
Lithuanian	Deksrazoksanas	Antraciklinių ekstravazacijų gydymas
Maltese	Dexrazoxane	Kura ta' estravażjoni ta' anthracycline
Polish	Deksrazoksan	Leczenie wynaczynienia antracyklin
Portuguese	Dexrazoxane	Tratamento dos extravasamentos de antraciclinas
Romanian	Dexrazoxan	Tratamentul extravazărilor antraciclinelor
Slovak	Dexrazoxan	Liečba extravazácií antracyklínu
Slovenian	Deksrazoksan	Zdravljenje ekstravazacije antraciklina
Spanish	Dexrazoxane	Tratamiento de las extravasaciones de antraciclinas
Swedish	Dexrazoxan	Behandling av extravasationer efter anthracykliner

[1] At the time of transfer of sponsorship.