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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Doxorubicin hydrochloride (in heat-sensitive liposomes) for the treatment of hepatocellular carcinoma

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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 23 February 2011, orphan designation (EU/3/10/833) was granted by the European Commission to Biological Consulting Europe Ltd, United Kingdom, for doxorubicin hydrochloride (in heat-sensitive liposomes) for the treatment of hepatocellular carcinoma.

What is hepatocellular carcinoma?

Hepatocellular carcinoma is a primary cancer of the liver (a cancer that starts in the liver, rather than a cancer that has spread to the liver from another location in the body). It is more common in men than in women, and occurs mostly in people who have scarring of the liver (cirrhosis) or after infection with the hepatitis B or C viruses. Symptoms of the disease include pain and swelling in the abdomen, weight loss, weakness, loss of appetite and nausea (feeling sick).

Hepatocellular carcinoma is a severe and life-threatening disease that is associated with very poor long-term survival.



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

At the time of designation, hepatocellular carcinoma affected less than 1 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 51,000 people*, and is below the ceiling 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 designation, several medicines were authorised in the EU for the treatment of hepatocellular carcinoma. The choice of treatment depended mainly on how advanced the disease was. Surgery to remove the tumour and liver transplantation were the only ways to cure the cancer, but could only be carried out in very few patients. Other treatments included radiotherapy (treatment with radiation), chemotherapy (medicines to treat cancer) and immunotherapy (medicines that stimulate the immune system to kill the cancer cells). Radiofrequency ablation (using a probe placed into the tumour to heat and destroy cancer cells) was also used to remove small tumours.

The sponsor has provided sufficient information to show that doxorubicin hydrochloride (in heat-sensitive liposomes) might be of significant benefit for patients with hepatocellular carcinoma because it is a new formulation of doxorubicin (an anticancer medicine that has been available since the 1960s), which is expected to be used in combination with radiofrequency ablation to improve the treatment of patients with this condition. This assumption will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

How is this medicine expected to work?

Doxorubicin is a cytotoxic (cell-killing) medicine that belongs to the group 'anthracyclines'. It works by interfering with the DNA within cells, preventing them from making more copies of DNA and making proteins. This means that cancer cells cannot divide and replicate, and they eventually die.

In this medicine, the doxorubicin is contained within microscopic fat particles called 'liposomes', which allow the medicine to accumulate mainly in the liver. The liposomes used in this medicine are heat-sensitive particles that release the doxorubicin when their temperature reaches 39.5°C. When this medicine is used together with radiofrequency ablation, the heat from the probe provokes the release of doxorubicin within the tumour, which is expected to improve the anti-tumour effects of this treatment.

What is the stage of development of this medicine?

The effects of doxorubicin hydrochloride (in heat-sensitive liposomes) have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with this medicine in patients with hepatocellular carcinoma were ongoing.

At the time of submission, doxorubicin hydrochloride (in heat-sensitive liposomes) was not authorised anywhere in the EU for hepatocellular carcinoma.

Orphan designation of this medicine had been granted in the United States of America for this condition.

*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 (EU 27), Norway, Iceland and Liechtenstein. At the time of designation, this represented a population of 507,700,000 (Eurostat 2011).

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 10 November 2010 recommending the granting of this designation.

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

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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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Doxorubicin hydrochloride (in heat-sensitive liposomes)	Treatment of hepatocellular carcinoma
Bulgarian	Доксорубицин хидрохлорид (в термочувствителни липозоми)	Лечение на хепатоцелуларен карцином
Czech	Doxorubicin hydrochlorid (v tepelně-senzitivní liposomální formě)	Léčba hepatocelulárního karcinomu
Danish	Doxorubicin hydrochlorid (i varmefølsomme liposomer)	Behandling af hepatocellulært carcinom
Dutch	Doxorubicinehydrochloride (in hitte-gevoelige liposomen)	Behandeling van hepatocellulair carcinoom
Estonian	Doksoorubitsiinvesinikkloriid (kuumustundlikkes liposoomides)	Hepatotsellulaarse kartsinoomi ravi
Finnish	Doksoorubisiinihydrokloridi (lämpöherkissä liposomeissa)	Hepatosellulaarisen karsinooman hoito
French	Chlorhydrate de doxorubicine (dans des liposomes thermo-sensibles)	Traitement du carcinome hépatocellulaire
German	Doxorubicinhydrochlorid (eingeschlossen in hitzelabilen Liposomen)	Behandlung des Leberzellkarzinoms
Greek	Υδροχλωρική δοξορουβικίνη (σε θερμοευαίσθητα λιποσώματα)	Θεραπεία του ηπατοκυτταρικού καρκινώματος
Hungarian	Doxorubicin-hidroklorid (hőre érzékeny liposzómába zárva)	Hepatocelluláris carcinoma kezelése
Italian	Doxorubicina cloridrato (in liposomi termosensibili)	Trattamento del carcinoma epatocellulare
Latvian	Doksoorubicīna hidrohlorīds (siltuma jūtīgās liposomās)	Hepatocellulāras karcinomas ārstēšana
Lithuanian	Doksoorubicino hidrochloridas (karščiui jautrių liposomų)	Hepatoceliulinės karcinomos gydymas
Maltese	Doxorubicin hydrochloride (liposomi sensitivi għas-sħana)	Kura tal-karċinoma epatoċellulari
Polish	Doksoorubicyny chlorowodorek (w termo-wrażliwych liposomach)	Leczenie raka wątrobowokomórkowego
Portuguese	Cloridrato de doxorubicina (em liposomas termosensíveis)	Tratamento do carcinoma hepatocelular
Romanian	Clorhidrat de doxorubicină (în lipozomi termosensibili)	Tratamentul carcinomului hepatocelular
Slovak	Doxorubicinhydrochlorid (v lipozómoch senzitívnych voči teplu)	Liečba hepatocelulárneho karcinómu
Slovenian	Doksoorubicin hidroklorid (v toplotno občutljivih liposomih)	Zdravljenje hepatocelularnega karcinoma
Spanish	Doxorubicina clorhidrato (en liposomas termosensibles)	Tratamiento del carcinoma hepatocelular

¹ At the time of designation

Language	Active ingredient	Indication
Swedish	Doxorubicinhydroklorid (i värmekänsliga liposomer)	Behandling av hepatocellulärt karcinom
Norwegian	Doksorubicinhydroklorid (i varmesensitive liposomer)	Behandling av hepatocellulært karsinom
Icelandic	Doxórúbicín hýdróklóríð (í hita-næmum lípósómum)	Meðferð við lifrarfrumukrabbameini