



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

## Public summary of opinion on orphan designation

### N'-(5-chloro-2-hydroxy-3-methylbenzylidene)-2,4-dihydroxybenzhydrazide for the treatment of partial deep dermal and full thickness burn wounds

On 22 September 2008, orphan designation (EU/3/08/568) was granted by the European Commission to Innate Pharmaceuticals AB, Sweden, for N'-(5-chloro-2-hydroxy-3-methylbenzylidene)-2,4-dihydroxybenzhydrazide for the treatment of partial deep dermal and full thickness burn wounds.

Innate Pharmaceuticals AB changed name to Creative Antibiotics Sweden AB in November 2010.

#### **What are partial deep dermal and full thickness burn wounds?**

Partial deep dermal and full thickness burns are deep burns to the skin. The wounds caused by partial deep dermal burns have blisters, and a pale white or yellow colour. Full thickness burns involve all of the skin layers, including the layer of fat under the skin. The wounds are painful and the skin appears dry and leathery, and is no longer elastic. These wounds can become infected with bacteria.

Partial deep dermal and full thickness burns can be life-threatening due to infection and the loss of fluids.

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

At the time of designation, partial deep dermal and full thickness burn wounds affected approximately 1 in 10,000 people in the European Union (EU)\*. This is equivalent to a total of around 50,000 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?**

Most partial deep dermal and full thickness burns greater than 3 cm in diameter are best treated with surgery soon after the burn to remove the dead tissue and replace it with healthy skin taken from

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\*Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed based on data from the European Union (EU 27), Norway, Iceland and Liechtenstein. This represents a population of 502,282,000 (Eurostat 2008).



elsewhere on the body. Many antimicrobial agents and disinfectants are also authorised and used in the EU to treat infections in burn wounds.

Satisfactory argumentation has been submitted by the sponsor to justify the assumption that N'-(5-chloro-2-hydroxy-3-methylbenzylidene)-2,4-dihydroxybenzhydrazide might be of potential significant benefit for the treatment of partial deep dermal and full thickness burn wounds because it has a new mechanism of action. This assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

### **How is this medicine expected to work?**

This medicinal product is expected to act by blocking the 'virulence' of bacteria such as *Pseudomonas aeruginosa*. Virulence is the ability of bacteria to cause harm and infection. The medicinal product is expected to do this by stopping the bacteria from injecting their enzymes into human cells.

### **What is the stage of development of this medicine?**

The effects of N'-(5-chloro-2-hydroxy-3-methylbenzylidene)-2,4-dihydroxybenzhydrazide have been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials in patients with partial deep dermal and full thickness burn wounds had been initiated.

N'-(5-chloro-2-hydroxy-3-methylbenzylidene)-2,4-dihydroxybenzhydrazide was not authorised anywhere worldwide for partial deep dermal and full thickness burn wounds or designated as an orphan medicinal product elsewhere for this condition, at the time of submission.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 9 July 2008 recommending the granting of this designation.

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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:

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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 languages<sup>1</sup>, Norwegian and Icelandic

Language	Active ingredient	Indication
English	N'-(5-chloro-2-hydroxy-3-methylbenzylidene)-2,4-dihydroxybenzhydrazide	Treatment of partial deep dermal and full thickness burn wounds
Bulgarian	N'-(5-хлоро-2-хидрокси-3-метилбензилиден)-2,4-дихидроксибензхидразид	Лечение на частични дълбоки кожни и подкожни рани от изгаряния
Czech	N'-(5-chlor-2-hydroxy-3-methylbenzyliden)-2,4-dihydroxybenzhydrazid	Léčba hluboké popáleniny kůže a podkožní tkáně
Danish	N'-(5-chlor-2-hydroxy-3-methylbenzyliden)-2,4-dihydroxybenzhydrazid	Behandling af partielle dybe dermale og subdermale forbrændinger
Dutch	N'-(5-chloro-2-hydroxy-3-methylbenzylidene)-2,4-dihydroxybenzohydrazide	Behandeling van diepe dermale en subdermale brandwonden
Estonian	N'-(5-kloro-2-hüdroksü-3-metüülbensülideen)-2,4-dihüdroksübenshüdratsiid	Sügavate dermaalsete ja kõiki nahakihte läbivate põletushaavade ravi
Finnish	N'-(5-kloori-2-hydroksi-3-methyylibensyliideeni)-2,4-dihydroksibenshydratsiidi	Syvien osittaisten dermaalisten ja subdermaalisten palovammojen hoito
French	N'-(5-chloro-2-hydroxy-3-méthylbenzylidène)-2,4-dihydroxybenzhydrazide	Traitement des brûlures dermiques intermédiaires et profondes
German	N'-(5-Chlor-2-Hydroxy-3-methylbenzyliden)-2,4-Dihydroxybenzhydrazid	Behandlung von tiefe dermale und subdermale Verbrennungen
Greek	N-(5-χλωρο-2-υδροξύ-3-μεθυλβενζυλιδέν)-2,4-δυσδροξιβενζυδραζιδη	θεραπεία των βαθιών εγκαυμάτων μερικού παχους και των εγκαυμάτων ολικού πάχους
Hungarian	N'-(5-kloro-2-hidroxi-3-metilbenzilidén)-2,4-dihidroxibenzhidrazid	Mély dermális és szubdermális égési sérülések kezelése
Italian	N'-(5-cloro-2-idrossi-3-metilbenzilidene)-2,4-diidrossibenzidrazide	Trattamento delle ustioni di secondo grado profonde e delle ustioni di terzo grado
Latvian	N'-(5-hloro-2-hidroksi-3-metilbenzilidēn)-2,4-dihidroksibenzhidrazīds	Dziļā dermāla un pilna ādas biezuma apdeguma ārstēšana
Lithuanian	N'-(5-chloro-2-hidroksi-3-metilbenziliden)-2,4-dihidroksibenzhidrazidas	Gilių odos ir poodinių audinių nudegiminių žaizdų gydymas
Maltese	N'-(5-chloro-2-hydroxy-3-methylbenzylidene)-2,4-dihydroxybenzhydrazide	Kura ta' feriti minn ħruq li jkunu parzjalment profondi fil-ġilda u fil-ħxuna kollha tal-ġilda
Polish	N'-(5-chloro-2-hydroksy-3-metylobenzylideno)-2,4-dihydroksybenzhydrazyd	Leczenie głębokich skórných i podskórných oparzeń
Portuguese	N'-(5-cloro-2-hidroxi-3-metilbenzilideno)-2,4-dihidroxibenzhidrazida	Tratamento de queimaduras profundas dérmicas e subdérmicas

<sup>1</sup> At the time of designation

Language	Active ingredient	Indication
Romanian	N'-(5-clor-2-hidroxi-3-metilbenziliden)-2,4-dihidroxibenzhidrazidă	Tratamentul arsurilor de gradul II parțiale profunde și a celor de gradul III
Slovak	N'-(5-chlór-2-hydroxy-3-metylbenzylidén)-2,4-dihydroxybenzhydrazid	Liečba hlbokých popálenin kože a podkožného tkaniva
Slovenian	N'-(5-klor-2-hidroksii-3-metilbenziliden)-2,4-dihidroksibenzhidrazid	Nega globokih kožnih in podkožnih opeklin
Spanish	N'-(5-cloro-2-hidroxi-3-metilbenzilideno)-2,4-dihidroxibenzohidrazida	Tratamiento de las quemaduras de segundo grado dérmicas profundas y de tercer grado
Swedish	N'-(5-klor-2-hydroxi-3-metylbensyliden)-2,4-dihydroxibenshydrazid	Behandling av partiella djupa dermala och subdermala brännskador
Norwegian	N'-(5-klor-2-hydroksy-3-metylbenzyliden)-2,4-dihydroksybenzhydrazid	Behandling av dype dermale og subdermale brannskader
Icelandic	N'-(5-klór-2-hýdroxíð-3-methýlbenzýliden)-2,4-tvíhýdroxýbenzhýdrazíð	Meðhöndlun annars og þriðja stigs bruna