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ABS Centelles

MEMORIA D'ACTIVITAT

D'INVESTIGACIÓ 2012

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Juny 2013

ANNEX 2

26-27 MARÇ 2012 INSPECCIÓ DE LES AUTORITATS JAPONESES DEL MEDICAMENT

薬機発第 0712016 号
平成 24 年 7 月 12 日

医薬品 GCP 実地調査結果通知書

CAP Centelles
Investigator 殿

独立行政法人医薬品医療機器総合機構理事長

平成 24 年 3 月 26 日から平成 24 年 3 月 27 日に実施した下記の医薬品 GCP 実地調査の結果について、改善すべき事項を別添のとおり通知します。

記

1．調査対象品目名

シーブリ吸入用カプセル５０μｇ
（一般名：臭化グリコピロニウム、コード記号：NVA237）
申請日：平成 23 年 11 月 25 日

2．調査対象承認申請資料名

5.3.5.1-2 A 26-week treatment, randomized, double-blind, placebo-controlled, parallel group study to assess the efficacy, safety and tolerability of NVA237 in patients with chronic obstructive pulmonary disease

別添（CAP Centelles）

1．承認申請資料の評価結果のもととなった医薬品 GCP に不適合である事項

特になし。

2．改善すべき事項

以下の事項が認められたため、医薬品 GCP を遵守して治験を実施すること。

（1）全般に関する事項

特になし

（2）個別症例に関する事項

1）治験実施計画書の除外基準（臨床症状のある前立腺肥大症）に抵触する被験者（Patient No. A2304/0131/00017）が治験に組み入れられていたことから、治験責任医師等は、治験に参加を求めることの適否について慎重に検討した上で、被験者となるべき者を選定すべきであった。

（平成 9 年厚生省令第 28 号※（以下「GCP」という。）第 44 条）

※治験実施当時に適用された GCP 省令である。

2）以下のとおり、治験実施計画書からの逸脱が認められた事から、治験責任医師当は、治験実施計画書を遵守して治験を実施すべきであった。

（GCP 第 46 条第 1 項）

ア．Patient No. A2304/0131/00030 において、治験薬割付時に無作為層別化の割付因子の一部が誤って登録されていた件

イ．Baseline Dyspnea Index (BDI)及び Transition Dyspnea Index (TDI)評価が、独立した評価担当者により実施されていなかった件

3）以下のとおり、症例報告書の記載が原資料と矛盾していた症例が認められたことから、治験責任医師等は、治験実施計画書に従って正確な、かつ、原資料を矛盾しない症例報告書を作成すべきであった。

（GCP 第 47 条第 1 項）

ア．Patient No. A2304/0131/00018 において、症例報告書に「筋拘縮」が有害事象として記載されていなかった件

イ．Patient No. A2304/0131/00028 において、症例報告書に「頭痛」が有害事象として、「Paracetamol STADA 1g」が併用薬として記載されていなかった件

ウ．Patient No. A2304/0131/00030 において、症例報告書に「爪甲真菌症」が有害事象として、「Odenil solucion PARA UNAS 5mL」及び「Ketoisdin 2% 100mL」が併用薬として記載されていなかった件

(Tentative translation)
This English document has been prepared for reference purpose only. In the event of inconsistency between the Japanese original and the English translation, the former shall prevail.

PMDA No. 0712016
July 12, 2012

Notification of the Result of GCP Inspection‡

To Investigator at CAP Centelles

From: Chief Executive
Pharmaceuticals and Medical Devices Agency

This is to inform you of the result of the inspection for compliance with the GCP for drugs ("GCP"), which was conducted on March 26 and 27, 2012, in relation to the following investigational product. The findings requiring corrective actions will be shown in the attachment.

1. Investigational Product

Seebri Inhalation Capsules 50 μg
(Active ingredient: Glycopyrronium bromide, Product code: NVA237)
Date of submission: November 25, 2011

2. Clinical Trial(s) Inspected

5.3.5.1-2 CNVA237A2304
A 26-week treatment, randomized, double-blind, placebo-controlled, parallel group study to assess the efficacy, safety and tolerability of NVA237 in patients with chronic obstructive pulmonary disease

‡ The provision numbers of the applicable Japanese regulation are given for the finding(s) requiring corrective actions in the original Notification of the Result of GCP Inspection. In this English translation, however, the relevant section numbers of the ICH GCP Guideline are also provided for reference purpose.

(Tentative translation)

This English document has been prepared for reference purpose only. In the event of inconsistency between the Japanese original and the English translation, the former shall prevail.

Attachment (CAP Centelles)

1. Critical finding(s) of GCP non-compliance that form the basis for the overall result of the inspection regarding the clinical trial data submitted.

No major problems were found.

2. Finding(s) requiring corrective actions

The following findings were identified. Clinical trials should be conducted in compliance with GCP*.

**In Japan, the applicable regulation is the Ordinance of the (then) Ministry of Health and Welfare No. 28 of 1997 (i.e. the Ministerial Ordinance on Good Clinical Practice for Drugs; hereinafter referred to as "J-GCP"). Although J-GCP is revised from time to time, the version referred in this inspection is the one that was applicable during the clinical trial period.*

(1) General finding(s)

No major problems were found.

(2) Finding(s) for individual subjects

1) The subject (Patient No. A2304/0131/00017) was enrolled in the clinical trial although the exclusion criteria (symptomatic prostatic hyperplasia) were met. The investigator and subinvestigators should select prospective subjects after they carefully examine whether or not it is appropriate to recruit the prospective subjects into the clinical trial.

(Article 44 of J-GCP)
(Section 4.5.1 of ICH GCP Guideline)

2) Some protocol deviations were found as listed below. The investigator and subinvestigators should conduct the clinical trial in compliance with the protocol.

(Article 46, Paragraph 1 of J-GCP)
(Section 4.5.1 of ICH GCP Guideline)

a. Patient No. A2304/0131/00030: At the time of treatment assignment, some erroneous entries were made with respect to the factors for stratified randomization.

b. Baseline and transition dyspnea indices (BDI/TDI) were not assessed by an independent, trained assessor.

3) The data reported on the case report form (CRF) was not consistent with the source documents as listed below.

The investigator and subinvestigators should accurately report the data, which are consistent with the source documents, on the CRF in accordance with the protocol.

(Article 47, Paragraph 1 of J-GCP)
(Section 4.9.2 of ICH GCP Guideline)

a. Patient No. A2304/0131/00018: "Muscular contracture" was not reported on the CRF as the adverse event.

b. Patient No. A2304/0131/00028: "Headache" for the adverse event and "paracetamol STADA 1 g" for the concomitant medication were not reported on the CRF.

c. Patient No. A2304/0131/00030: "Onychomycosis" for the adverse event, and "odenil solucion PARAUNAS 5 mL" and "ketoisdin 2% 100 mL" for the concomitant medications were not reported on the CRF.