# A Multi-center Study to Evaluate the Pharmacokinetics of Diacerein and Rhein and the Safety of Diacerein after Maximum Use, Topical Administration of CCP-020 (Diacerein 1% ointment) to Patients with Epidermolysis Bullosa (EB)

Published: 30-04-2018
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| **Ethical review** | Not approved |
| **Status** | Will not start |
| **Health condition type** | Skin and subcutaneous tissue disorders congenital |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON46073

**Source**
ToetsingOnline

**Brief title**
CCP2101

### Condition

- Skin and subcutaneous tissue disorders congenital
- Epidermal and dermal conditions

**Synonym**
Epidermolysis Bullosa

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Castle Creek Pharmaceuticals, LLC
**Source(s) of monetary or material Support:** Castle Creek Pharmaceuticals;Inc.

## Intervention

**Keyword:** Diacerein, Epidermolysis Bullosa

## Outcome measures

### Primary outcome

Derived plasma PK parameters (Cmax, Tmax and AUC), if available, for diacerein and rhein will be summarized by treatment using descriptive statistics (sample size, arithmetic and geometric mean, CV%, SD of the arithmetic mean, median, minimum, and maximum)

### Secondary outcome

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# Study description

### Background summary

Epidermolysis bullosa (EB) is a rare, genetic skin disease characterized by fragility of the skin and mucous membranes resulting in painful blisters and erosions after minor trauma, and is associated with significant morbidity and mortality. EB is both a pediatric and an adult disease that tends to affect younger patients most severely. Diacerein 1% Ointment is a topical ointment containing diacerein (4,5-bis[acetyloxy]-9,10 dihydro-9,10-dioxo-2-anthracene carboxylic acid, also known as diacetyl-rhein), a highly purified anthraquinone derivative, and is being developed for the treatment of EB.

Diacerein in the topical formulation is hydrolyzed to rhein in the epidermis and dermis following administration. Diacerein and rhein have been shown to inhibit the in vitro and in vivo production and activity of interleukin-1*

(IL-1*) and other pro-inflammatory cytokines.

IL-1* is a pro-inflammatory cytokine that has been linked to a number of inflammatory and autoimmune diseases, including rheumatoid arthritis (RA), OA, hemophilic arthropathy, gouty arthritis, type 2 diabetes mellitus (T2DM), diabetic nephropathy (DN), and EB. In vitro and in vivo animal studies have shown that both diacerein and its active metabolite rhein inhibit the production and activity of pro-inflammatory and procatabolic cytokines such as IL-1 and IL-6, and the expression of inducible nitric oxide synthase (iNOS) and tumor necrosis factor-* (TNF-*).

**Study objective**

The primary objective of the study is to descriptively characterize the single-dose and steadystate
Pharmacokinetics (PK) of diacerein (if quantifiable) and its active metabolite, rhein, after topical application of CCP-020 (diacerein 1% ointment) under maximum use conditions in adolescent and adult patients with EB, and in infants/children with EB.

The secondary objective of the study is to assess the safety and tolerability of single-dose and
steady-state topical application of CCP-020 (diacerein 1% ointment) in patients with EB.

**Study design**

This is an open label, single period study in 16 to 20 patients with EB consisting of infants/children (ages 6 months * 11 years, inclusive) and adolescents/adults (ages 12 and up) with at least 6 subjects between the aged 6 months to 11 years, inclusive (infants/children). The
study will consist of two cohorts as follows:

1. 8-10 adolescent and adult patients with EB (aged 12 and older)
Lesions encompassing = 2% BSA for study entry. Diacerein application area to be = 5% BSA and include lesioned and non-lesioned skin (if lesions account for less than 5% BSA); however, topical administration must be =30% BSA.

2. 8-10 infants/children with EB (aged 6 months to 11 years, inclusive)
Lesions encompassing = 2% BSA for study entry. Diacerein application area to be = 5% BSA and include lesioned and non-lesioned skin (if lesions account for less than 5% BSA); however, topical administration must be =30% BSA.

**Intervention**

All subjects will be dosed open label with CCP-020 (Diacerein 1% ointment)

daily for 10 days.

**Study burden and risks**

Risks: possible side effects of the study medication Burden: blood draws, filling in diary, instructions on study drug and treatment of application area

# Contacts

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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

## Inclusion criteria

1. Subject/caregiver is able to comprehend and willing to sign an Informed Consent and/or Assent Form.
2. Subject is male or female at least 12 years of age (Cohort 1) or at least 6 months of age to 11 years, inclusive (Cohort 2) at screening.
3. The subject must weigh at least 9 kg (19.8 lbs) at Screening.
4. Subject has a documented genetic mutation consistent with EB. A blood or saliva sample will be collected for genetic confirmation if no documented gene mutation data is available.
5. Subject has EB lesions on * 2% body surface area (BSA) and the EB lesions are in the following body areas:
a. Localized: plantar and/or palmar areas
b. Generalized: arms, legs, torso, hands and feet.
6. Subject/caregiver agrees to not apply any other topical products to the application area during the treatment period
7. If the subject is a woman of childbearing potential, she has a negative urine pregnancy test and agrees to use an approved effective method of birth control, as defined by this protocol, for the duration of the study.
8. Subject is non-pregnant, non-lactating and is not planning for pregnancy during the study period
9. Subject is in good general health and free of any known disease state or physical condition which, in the investigator*s opinion, which exposes the subject to an unacceptable risk by study participation.
10. Subject is willing and able to follow all study instructions and to attend all study visits.

## Exclusion criteria

1. Subject has EB lesions where drug will be applied that are infected (i.e., EB lesions that require anti-microbial therapy to treat an infection)
2. Subject has used any diacerein containing product within 1 month prior to Visit 1
3. Subject has used systemic immunotherapy or cytotoxic chemotherapy within 60 days prior to dosing.
4. Subject has used systemic steroidal therapy or has used topical steroidal therapy on the EB lesions in the application area within 14 days prior to dosing (Note: inhaled, nasal sprays, and ophthalmic products containing steroids are allowed)
5. Subject has evidence of a systemic infection or has used systemic antibiotics within 7 days prior to dosing
6. Subject has used any systemic diuretics or cardiac glycosides or any systemic product that, in the opinion of the investigator, might put the subject at undue risk by study participation or interferes with the study medication application or the study assessments within 30 days prior to dosing
7. Subject has a current malignancy, or a history of treatment for a malignancy within 2 years prior to dosing (Note: does not include non-melanoma skin cancer)
8. Subject currently has diabetes mellitus (HbA1c *6.5%) Note: controlled diabetes (HbA1c < 6.5%) is also considered exclusionary
9. Subject has a history of cardiac, hepatic (ALT and or AST >2x ULN, Total bilirubin >1.5x ULN at Visit 1), or renal disease (eGFR<30 ml/min/1.73 m2 [MDRD-adults *18, Bedside

Schwartz * children <18]) that, in the opinion of the investigator, might put the subject at undue risk by study participation or interferes with the study medication application of the study assessments
10. Subject has an active non-EB skin disease (e.g., psoriasis, atopic dermatitis, eczema, sun damage, etc.), or condition (e.g., sunburn) that, in the opinion of the investigator, would put the subject at undue risk by study participation or would interfere with the study medication application or the study assessments
11. Subject has a history of sensitivity to any of the ingredients in the study medication
12. Subject has participated in an investigational drug trial in which administration of an investigational study medication occurred within 30 days prior to dosing

# Study design

## Design

**Study type:** Interventional

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| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Treatment |

## Recruitment

NL

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|---|---|
| Recruitment status: | Will not start |
| Enrollment: | 8 |
| Type: | Anticipated |

## Medical products/devices used

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|---|---|
| Product type: | Medicine |
| Brand name: | Diacerein 1% Ointment |
| Generic name: | Diacerein |

# Ethics review

Approved WMO

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| Date: | 30-04-2018 |
| Application type: | First submission |

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| Review commission: | CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag) |
| Not approved<br>Date: | 07-08-2018 |
| Application type: | First submission |
| Review commission: | CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag) |

# Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

| Register | ID |
|---|---|
| EudraCT | EUCTR2018-000439-29-NL |
| CCMO | NL65708.000.18 |