STUDY PROTOCOL OUTLINE

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Participating centers	100 dermatologists (community practice and hospital)
Country	France
Title	Multicenter, national non-interventional study including a registry and a prospective cohort of patients with common scab.
Rational and background	Scabies is a contagious skin disease caused by a mite known as Sarcoptes scabiei. It affects both men and women, all age groups, and all social circles. According to INVS, in 2001, its annual incidence in France was said to be 328 cases/100,000 inhabitants. It is mainly transmitted (95% of cases) via direct and frequent physical contact and, more rarely (5% of cases), via the environment (linen). The parasitic cycle is 10 to 15 days and consists of 4 stages (eggs, larvae, nymphs and adults). The infesting forms (fertilised females) lay two or three eggs per day. Females'life is 1 month.. Its clinical signs are constant itching increasing in the evenings and at night, and specific cutaneous lesions: burrow tracks, beaded blisters and scabietic nodules. Diagnosis is based on the presence of constant itching increasing at night, and specific cutaneous lesions. The diagnosis may be confirmed by direct parasitological tests (reference test) (evidencing the itch mite, larvae, eggs and scybals). A negative test does not rule out diagnosis. The condition may also be diagnosed by dermatoscopy in well trained physicians. Management involves treating the patient, the patient's family members and the environment. Treatment is administered topically or orally, although monotherapy is recommended by the HCSP (French Public Health Committee). Two treatments at a one-week interval are recommended for all forms of the infection. Family members receive the same treatment as the patient. In the event of classic scabies, individuals in the patient's immediate circle will be treated (persons having had prolonged skin contact with the affected patient) even if they have no symptoms. The infection is considered to be cured when itching disappears. Itching may persist for up to 4 weeks after treatment (cutaneous irritation, contact dermatitis, treatment failure). Out of the topical treatments, Ascabiol®(benzyl benzoate has been the pioneering product for the treatment of scabies since 1936, the standard of care in France. Due to a shortage of one of its active ingredients (monosulfiram), it was no longer available and marketing ceased in 2012. As from 2015, a major scabies epidemic, mainly due to the lack of topical alternatives to the oral form, caused the authorities to request the launch of a new formulation of Ascabiol® (according to a simplified procedure). The new formula of Ascabiol® (without monosulfiram) was relaunched in 2015 at the same time as another topical alternative (Permethrine). The application method for the new formulation (10% benzyl benzoate emulsion for cutaneous application) was modified relative to the previous formulation (lotion). Limited data on the efficacy and safety of Ascabiol® and on the conditions of use in actual practice are available. This study aims to provide these data in real life conditions.

Study Type	Phase IV non interventional observational study with a registry.
Study objectives	**Main objective**: to evaluate the% of patients cured on day 28 (±7 days) in patients with common scab and treated with Ascabiol® in real life conditions. **Secondary objectives**: to describe • Epidemiological and clinical characteristics of treated patients • Respect of the prescription methods (dosage and good use) of the 10% benzyl benzoate emulsion • treatment of the family • treatment of the environment • Predicting factors of treatment success at D28 □ 7 days (S4) • Recurrence rate at J84 (S12) and predictors of recurrence. • Registry data
Number of patients	1000 patients maximum in the registry in which 300 patients treated with ASCABIOL® (Cohort patients). Each physician may include up to 10 patients in the registry and up to 5 patients in the cohort.
Conduct of the study and data collection	**This study will include 2 phases:** • A registry containing all the epidemiological and clinical characteristics of patients fulfilling the participation criteria. All patients will be assessed on D0 regardless of the prescribed treatment. The study is observational; also the prescription of the treatment or not with Ascabiol® will be left to the appreciation of the evaluating physician. • A follow-up cohort: patients treated with Ascabiol® monotherapy and meeting the criteria for participation in follow-up will be more widely evaluated on D0 and reviewed on D28 (± 7 days). Patients considered to be cured on day 28 (± 7 days) will be contacted again by the examining physician at J84 (W12).
Criteria for participation and non-participation of patients	**Criteria for participation in the registry: all patients** - more than 1 month old - outpatient - visiting for untreated common scab - giving their oral consent to participation (over 18 years) or for which the parents give their participation agreement (under 18 years). **Criteria for participation in the cohort: all patients** - included in the registry - treated with Ascabiol® monotherapy **Criteria for non-participation in the registry and monitoring:** - known pregnancy - breastfeeding - hyperkeratotic scabies - scabies already treated in the last 6 months
Collected data	Participating physicians - CFR will collect: - Physican's details - Physician's characteristics: sex, age, specialty, type of practice (liberal, hospital, both practice) Patients participating in the registry (D0) For the duration of the study, when a patient fulfills the criteria for participation in the registry, the physician will propose to participate in this study, give him / her an information leaflet (or to parents). If he agrees to participate in the study (and / or the parents), the physician will proceed to visit D0 and complete the following data: - Verification of the criteria for participation in the registry - Date of the visit - Demographic characteristics of the patient (age, sex, weight, height) - Socioprofessional category (8 INSEE categories): 1: Farmers; 2: Craftsmen, tradesmen and entrepreneurs; 3: executives and higher intellectual professions; 4: Intermediate Professions; 5: Employees; 6: Workers; 7: Retired; 8: Other people without professional activity

	- Habitual place of residence: fixed domicile, residence or institution, homeless. - Characterization of the family home: o Number of people living under the same roof o Number of people belonging to the first circle: people who have had skin contact with a case (close family circle, sexual relations, nursing care, children's games) o Number of children - Type of anti-scabious treatment prescribed for the patient o Monotherapy (local or oral treatment) o Bitherapy (local and oral treatment) - Prescription adjuvant treatments o Antihistamine o Local corticoid o Soothing cream o None *For each patient included in the registry, when the physician decides to prescribe Ascabiol® as monotherapy it will include the patient in the cohort*. *Patients belonging to the same family home may be included if they are present at the consultation.* <u>Patients participating in the cohort: data collected (D0)</u> - Itching o Duration (days) o Intensity (VAS from 0 to 10) o With nocturnal awakenings (yes / no) o Location (scalp, face, abdomen, armpits, anterior thorax, upper back, lower back, arms, interdigital spaces, forearm, anterior cuffs, back of hands, palms, genital area, buttocks, thighs, legs, malleolar regions, back of the feet, soles of the feet). - Skin lesions o Scabious burrow tracks (yes / no) o Scabious nodules (yes / no) o Beaded vesicles (yes / no) o Eczematous lesions (yes / no) o Impetiginized lesions (yes / no) o Scratch lesions (yes / no) - Estimation of the skin surface on which lesions are visible: <20%; 21 to 40%; 41 to 60%; 61 to 80%; > 81%. (reference: a palm of the hand with the fingers = 1%) - Personal history of scabies (yes / no) - Context of the disease o Isolated case (no case in the entourage, unidentified origin of contamination) yes / no o Family case: yes / no o Epidemic (two or more cases of scabies have been diagnosed by a physician in hospital, possibly with other patients or caregivers): yes / no - Mode of confirmation of the diagnosis of scabies o Clinical diagnosis (yes / no) [if intimate with cases in the environment (marital or family characteristics are very suggestive) + pruritus (nocturnal recrudescence) + characteristic localization of skin lesions] o Dermatoscopy (yes / no); o Parasitological examination (yes / no). - Treatments o Modalities of treatment with Ascabiol® ▪ Prescription according to recommendations and SmPCs ▪ Number of vials prescribed ▪ Delivery of a written document (yes / no) ▪ Oral explanations (yes / no) o Number of people in the 1st circle with pruritus and for whom an anti-scabious prescription has been done (in addition to the patient's) o Number of people in the 1st circle who do not have pruritus and for whom an anti-scabious prescription has been done (in addition to that of the patient) o Recommendations made for linen (yes / no) ▪ Delivery of a written document (yes / no)

	o Recommendations made for the treatment of the environment ▪ Bed treatment recommendation (yes / no / NA) ▪ Sofa / chair treatment recommendation (yes / no / NA) ▪ Carpet treatment recommendation (yes / no / NA) ▪ Treatment recommendation for car seats (yes / no / NA) ▪ Acaricide prescription (yes / no / NA) (if yes, which one?) ▪ Delivery of a written document (yes / no / NA) o Hygiene measures and isolation prescribed in case of epidemic (yes / no / NA) <u>Visit at D28 (± 7 d)</u> - Intensity of pruritus (VAS from 0 to 10) - Compliance with Ascabiol's prescription and dosage instructions according to the SmPCs (yes / no) - Simultaneous treatment of all persons in the 1st circle (yes / no) - Treatment of the linen (yes / no) - Treatment of the environment (yes / no) - Number of vials prescribed sufficient (yes / no) - Clinical healing (cure will be defined as more than 75% decrease in pruritus intensity at day 28 (± 7 days) compared to day 0 or pruritus intensity at day 28 (± 7 days) less than 2 (on the scale from 0 to 10) + the clinical judgment of the physician) (yes / no) - Results: Dermatoscopy and / or parasitological examination if failure or relapse - Estimation of the skin surface on which lesions are visible: <20%; 21 to 40%; 41 to 60%; 61 to 80%; > 81%. (Reference: a palm of the hand with the fingers = 1%) Phone call to D84 (W12) Patients considered cured on day 28 (±7 days) will be contacted again by the examining physician at D84 (W12) to find out if the patient is still cured.
Test product	Ascabiol®
Adjunctive treatment	The Physician and the healthcare team participating in this study will be free of their prescription.
Endpoints (cohort)	The primary endpoint will be the % of patients cured on day 28 (±7 days). The secondary endpoints will be to describe; - Epidemiological and clinical characteristics of treated patients - Respect for Ascabiol's methods of prescription - Respect for caring for the family - Respect for the treatment of the environment - Predictors of healing at D28 (± 7 d) (W4) - Recurrence rate at D84 (W2) and predictors of recurrence - Registry data
Sample size	The number of subjects required was estimated on the precision to be obtained on the main end point. Assuming that 90% of patients treated on day 0 will be cured on day 28, a number of 282 patients will achieve a precision of about 3.5%. This number is raised to 300 to account for any patients lost to follow-up.
Statistical analyses	The analysis of the primary endpoint will be conducted on all patients included in the cohort and reviewed at D28 (±7 days). The 95% confidence interval will be calculated. Sensitivity analyzes will be conducted. Secondary end points: the analyzes of the secondary end points will be descriptive. The search for predictors of treatment failure on day 28 (W4) and recurrence on day 84 (W12) will be done by univariate analyzes to select the factors to be considered in a multivariate logistic regression model.

Study's agenda	Regulatory Phase: July to October 2018 Physician Recruitment: October to November 2018 Implementation of the study: October to December 2018 Inclusion period: November 2018 to May 2019 End of the follow-up at 1 month: June 2019 End of 3-month follow-up: September 2019 Data management: February to October 2019 Statistical analysis: November 2019 2nd scientific committee: December 2019 Study report: January - February 2020 Publication: Q1 2020