

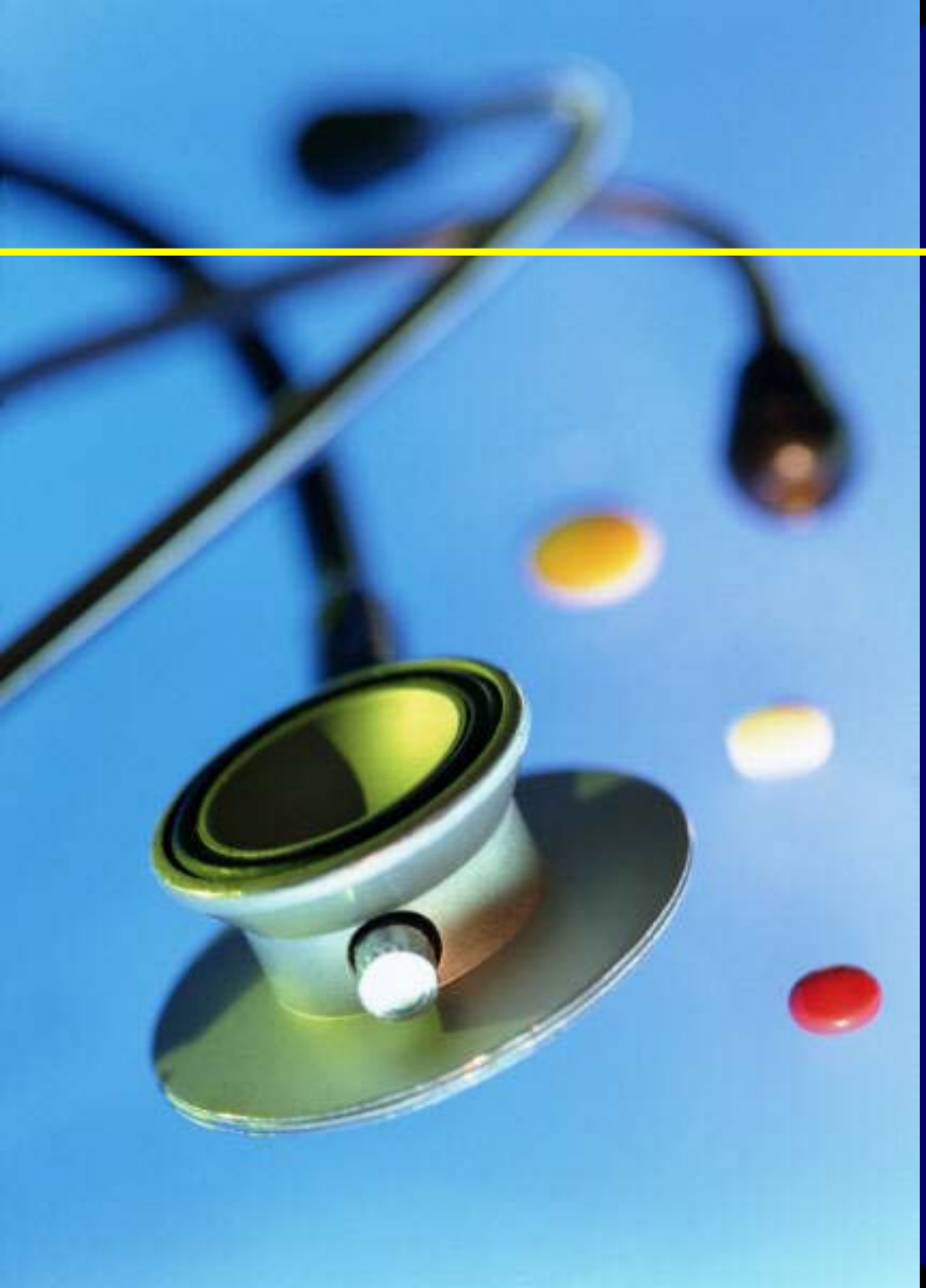
https://dspace.org/

Informed consent methods: an analysis of volunteer understanding

Jacobs, Janine

2009-02-26T08:14:52Z
http://hdl.handle.net/10539/6494

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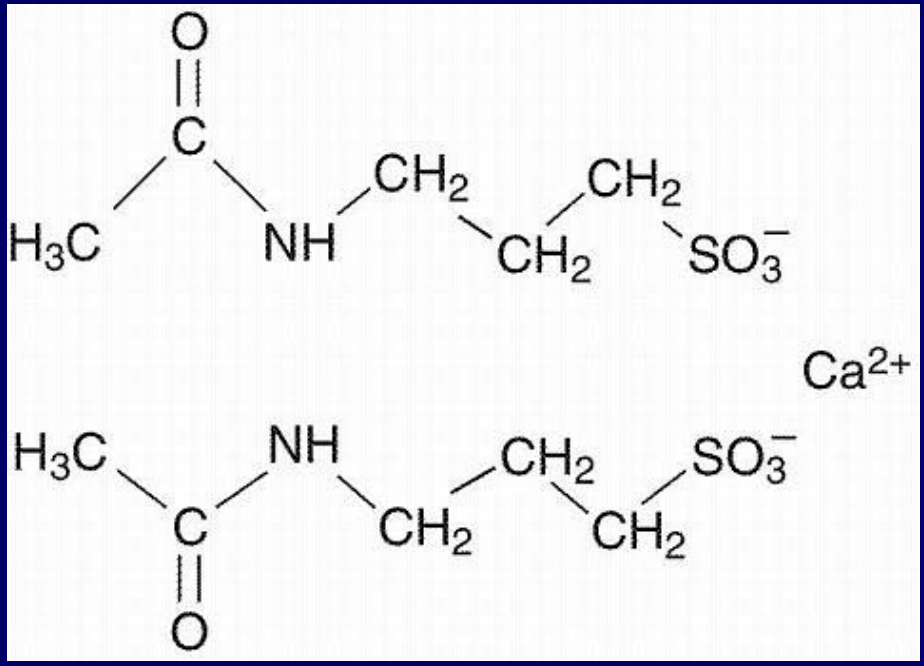


PAREXEL.

AN OPEN-LABEL, 4-WAY CROSSOVER BIOAVAILABILITY STUDY TO COMPARE THREE DIFFERENT FORMULATIONS OF ACAMPROSATE CALCIUM 666 mg (6x111mg tablets) WITH BESOBRIAL® 666 mg (2x333mg tablets) IN HEALTHY VOLUNTEERS

Definitions

- OPEN LABEL
- 4 WAY CROSSOVER
- BIOAVAILABILITY
- ACAMPROSATE CALCIUM
- BESOBRIAL



Acamprosate Calcium structure

Tests to determine eligibility

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- Height and weight measurements
- Urine test
- Urine screen for drugs of abuse
- Alcohol breath test
- Blood pressure, pulse rate and body temperature observations
- Electrocardiogram (ECG)
- Chest X-ray
- Laboratory investigations: Full blood count, clinical chemistry profile and HIV and hepatitis B and C tests.
- A full medical history and information on alcohol and tobacco consumption

DRUGS OF ABUSE TESTS (to determine eligibility)

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- Exclusion due to positive test
- Positive tests may be repeated at the discression of the doctor

HIV AND HEPATITIS B AND C INFORMATION

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- Disease might cause symptoms and signs that could be mistaken for adverse events due to the study medication - study results worthless
- Study medication could dangerously aggravate conditions, such as HIV or Hepatitis
- Advantages in knowing HIV & Hepatitis status
- In case of a positive test, you will be informed by the study doctor or appropriately qualified designee
- Results are strictly confidential



Note: Feel free to discuss any questions with the study doctor

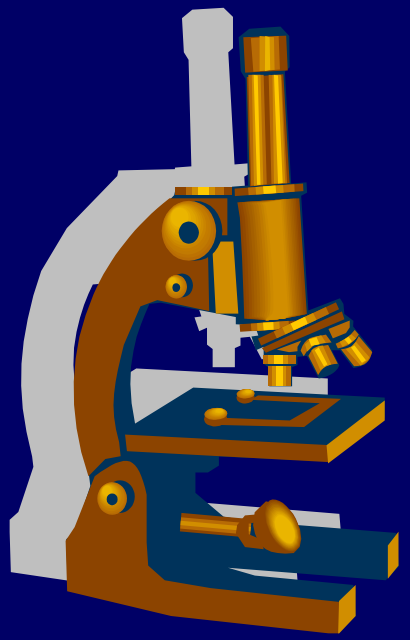
Introduction

Sponsor: Somaxon Pharmaceuticals, Inc.

Participation: Voluntary

Withdrawal:

- Any time upon your request
- Upon recommendation of the doctor
- If you do not comply to the protocol
- You need to undergo laboratory investigations



Purpose of the study

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- Compare blood levels and safety of 4 preparations of medicine
- 1 preparation already in use for alcohol abstinence (reference product)
- 3 new preparations (test product)
- ALL preparations contain the same active ingredient
- PURPOSE: To compare the 4 products with regard to the amount of medication that gets into your blood and is available for your body to use

Regulatory Authorities

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- Committee for Medical Research of The University of the Free State
- South African Medicines Control Council (MCC)
- Declaration of Helsinki

Information on the study medication

- 4 different acamprosate calcium tablet products
- You will receive one of these 4 products during the treatment phase
- Dosage = 666mg per phase

  3 phases = 6 x 111mg

  1 phase = 2 x 333mg
- Acamprosate calcium- treatment of alcohol abuse, to abstain from alcohol



Dosage of Acamprosate Calcium

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USUAL DOSAGE

- 2 x 333mg 3 times daily



STUDY DOSAGE:

- 1 x 666mg in the morning per phase by mouth

Potential side-effects

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Body as a whole

- Accidental injury (including fractures),
- weakness,
- pain,
- headache,
- abdominal pain (stomach pain),
- back pain,
- infection,
- flu syndrome,
- chest pains,
- chills (feeling cold),
- suicide attempt



Potential side-effects

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Digestive system

- Diarrhea,
- flatulence (excessive gas in the stomach),
- nausea,
- vomiting,
- indigestion,
- constipation,
- lack of or increased appetite.

Potential side-effects

PAREXEL.

Nervous system

- Anxiety (including nervousness),
- depression,
- dizziness,
- dry mouth,
- sleeplessness,
- sleepiness,
- paresthesia (“pins and needles”, especially involving the face and extremities),
- decreased libido (decreased sexual drive),
- forgetfulness,
- thinking abnormal,
- quivering (shaking),
- vasodilatation (widening of the arteries),
- hypertension (high blood pressure).

Potential side-effects

PAREXEL.

Skin and appendages

- Pruritus (itchiness),
- sweating,
- Rash

Cardiovascular system

- Palpitation (a sensation of feeling the heart beating rapidly),
- syncope (brief lapse in consciousness)

Potential adverse events

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Metabolic and nutritional disorders

- Peripheral edema (swelling of the extremities/lower limbs),
- weight gain

Muskuloskeletal system

- Myalgia (muscle pain),
- arthralgia (joint pain)

Special senses

- Abnormal vision,
- taste perversion (abnormal taste disorder)

Potential adverse events

PAREXEL.

Respiratory system

- Rhinitis (inflammation of the mucous membranes of the nose),
- increased cough,
- dyspnea (shortness of breath),
- pharyngitis (inflammation of the throat),
- bronchitis (inflammation of the mucous membrane in the bronchial tubes)

Urogenital system

- Impotence (unable to achieve an erection)

Potential adverse events

Less frequent and unexpected adverse events not mentioned above cannot be excluded.

Discuss any questions with your doctor

Allergic reactions

Cannula may cause:

- Irritation
- Inflammation
- Clot formation



Contra-indications

- patients who previously have shown hypersensitivity (allergic reactions) to acamprosate calcium or any of its ingredients,
- women who are pregnant or breastfeeding,
- patients with severe liver or kidney disease.



Study Performance

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Time	Phase 1	Phase 2	Phase 3	Phase 4
12 Hrs prior to dose	Report to study centre	Report to study centre	Report to study centre	Report to study centre
0 Hrs	Receive medicine	Receive medicine	Receive medicine	Receive medicine
48 Hrs	Discharge from study centre	Discharge from study centre	Discharge from study centre	Discharge from study centre
60 Hrs	Return to study centre for blood draw	Return to study centre for blood draw	Return to study centre for blood draw	Return to study centre for blood draw

14-21 Days Washout → **14-21 Days Washout** → **14-21 Days Washout**

Study Performance

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The following tests will be done upon admission:

- alcohol breath test and urine screen for drugs of abuse
- urine sample and blood samples, repeated 24hrs after dose and at the end of study
- body temperature, pulse rate and blood pressure, repeated before administration of medicine
- ECGs (cardiac tracings) before administration of study medication
- Pulse rate, blood pressure recordings and ECGs will be repeated at approximately 2, 4, 6, 24, 48 & 60 hours post-dose, and body temperature at 12 hours post-dose of Phases 1, 2, 3, and 4

Study Performance

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- receive the study medication at 07:30* with 240 mL water
- sit on your bed for 2 hours
- 4 mL (approximately 1 teaspoon) each, through a cannula (small plastic tube) inserted in a vein in your forearm
- If the cannula is removed, samples will be collected by venipuncture (drawing blood from a vein using a needle and syringe)
- Sixteen blood samples (64 mL) will be collected over 60 hours (i.e. each phase)
- Lab investigations before and after study = 95 mL (19 teaspoons)
- Total = will not exceed 351 mL (approximately 1.5 cups) (excluding repeats)

** The time of dosing commencement may vary due to logistical reasons.*

Precautions and emergency measures

- supervision for the first 48 hours after administration
- Should you experience any adverse events you will receive all the necessary medical treatment, even if the drug is withdrawn.

Restrictions

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Medicines (2 weeks prior before and during the study):

- Over the counter medicines (OTC)
- **If you need any medication, please report it immediately to your doctor**

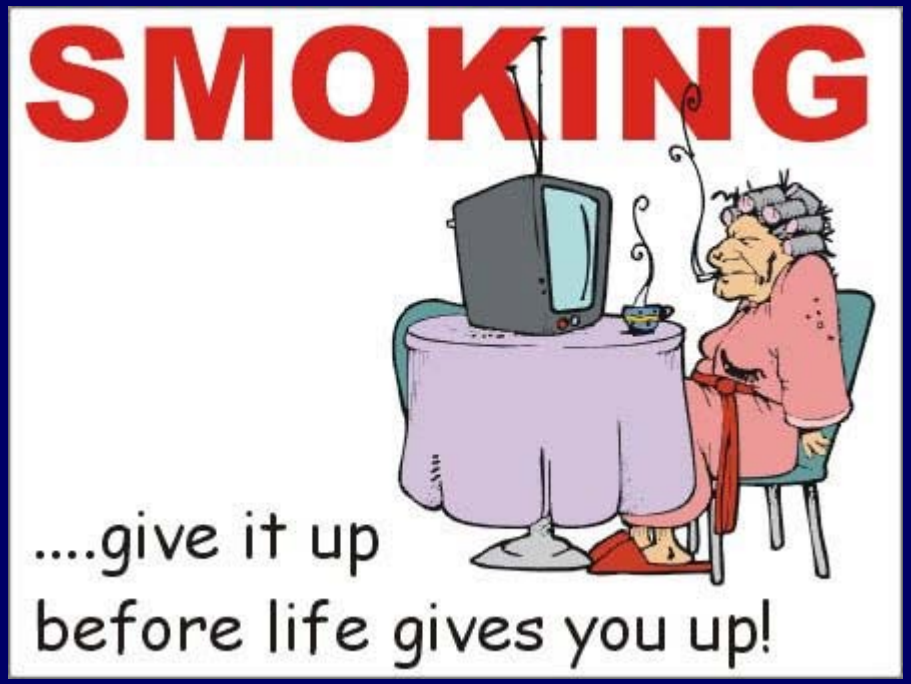


Restrictions

PAREXEL.

Smoking:

- Only non-smokers will be included in the study.



Restrictions

Diet:

3 Days before:

- fluids containing grapefruit

48 Hours before – 60 Hours after:

- methylxanthines e.g. caffeine

48 Hours before – end of study:

- No alcohol



Caution: Random alcohol tests may be done

Restrictions

PAREXEL.

- fast from approximately 10 hours before dosing
- only food allowed: during first 14 hours of the first clinic day- standardised meals at 5 and 10 hours, and a standardised snack 13 hours after administration of study medication
- 240 mL water approximately 90 minutes before medication administration, with medication administration, 2 and 4 hours after medication administration and 240 mL apple juice with the meals.
- You will receive a caffeine-free warm beverage (200 mL) 8 and 13 hours after medication administration.
- All food and beverages will be caffeine-free
- From 14 hours after medication administration, you may eat and drink any food and beverages, except for food and fluids containing caffeine or xanthines, which will not be allowed for the entire clinic stay (up to 48 hours post-dose) and grapefruit and/or alcohol

Restrictions

PAREXEL.

Physical exercise

- 24 hrs prior to administration
- 60 hrs post administration



FREQUENTLY USED CAFFEINE-CONTAINING FOOD AND BEVERAGES

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Not allowed 24 hours prior and 384hrs after administration:

- Coffee
- Tea
- Cola-flavoured drinks (e.g. Coke®)
- Cocoa
- Chocolate
- Caffeine-containing beverages (e.g. Red Bull®)







STUDY COMPLETION

- Within 72 hours of completion of the last phase of the study
- A physical examination and urinalysis as part of the post-study safety evaluation
- ECG if your post-study visit does not coincide with a 60 hour visit
- If certain laboratory investigations (haematological or clinical chemistry) have to be repeated, the project nurse will set a date and time for repeat tests
- If you are withdrawn from the study, a post-study physical examination and other investigations may be performed



Withdrawal Criteria

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You have the right to withdraw from the study at any time, irrespective of the reason, without detriment to your medical care.

The following are pre-defined incidents that may lead to your withdrawal from the study:

- Adverse events as a result of taking the study medication
- Illness requiring medication
- Protocol violation (wilful disobeying of the protocol instructions and restrictions, as communicated to you both verbally and in this document)
- Abnormally raised body temperature before administration of study medication on clinic days
- Positive testing for pregnancy
- If any of the alcohol breath tests test positive, further participation in the study will not be permitted

Remuneration

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- No cost implications on you for study procedures
- Loss of time and inconvenience as a result of participation
- No remuneration is applicable to the screening procedures
- If you do not complete: compensation proportional to time of participation.
- R9 400.00 (taxable)
- Violation of the protocol instructions: may result in forfeiture of remuneration (wilful disobeying of instructions communicated to you verbally and in writing)



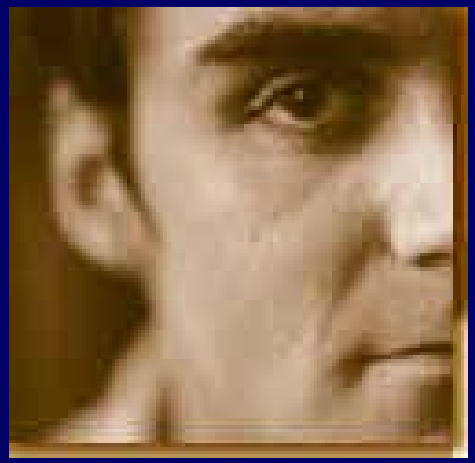
CONDITIONS OF INSURANCE COVERING CLINICAL STUDIES *(IN COMPLIANCE WITH ABPI GUIDELINES)*

PAREXEL.

- Insurance coverage: Santam limited, policy No. P00931
- Indemnification is provided without regard to the question of legal liability as long as it can be shown that participation in the study caused the death or disability.
- The insurer will determine the amount of money necessary to cover the difference between the actual financial status if neither death nor deterioration in health occurred and the resulting financial status. Any compensation received from social insurance schemes or other sources will be deducted from the amount of compensation provided through FARMOVS-PAREXEL.
- During the course of the clinical study you may not participate in any other study.
- Any deterioration in your health during or directly after the clinical study must be reported to the doctor at once. In the case of a serious adverse event, the doctor must notify the sponsor, Ethics Committee and the South African Medicines Control Council by telephone or facsimile within 24 hours of becoming aware of the occurrence of the event. The notification must be followed by a written report within 48 hours after the initial notification, or at the latest on the following working day. FARMOVS-PAREXEL will inform the insurance company in the event of a claim.
- Should you have to receive any medical care not pertaining to the study in question, this must be reported to the doctor.

Additional Information

- 36 male volunteers
- Duration: 9-12 weeks



Benefits

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You will not benefit directly from this study- only HEALTHY participants enrolled



Confidentiality

PAREXEL.

- Staff of FARMOVS-PAREXEL, the sponsor, and members of the Ethics Committee as well as the regulatory authorities will have access to all personal data pertaining to the study
- ALL findings: strictly confidential
- Data may be reported in scientific journals/meetings, but you will not be identified
- You will be informed in a timely manner when new information becomes available that may influence your willingness to continue participation in the study

Questions

PAREXEL.

