## Clinical Trial Details

### CTRI Number
CTR/2011/05/001709 [Registered on: 05/05/2011] -Trial Registered Prospectively

### Last Modified On
20/01/2012

### Type of Trial
BA/BE

### Study Design
Randomized, Crossover Trial

### Public Title of Study
A bioequivalence study of single oral dose of three brands of 300mg Phenytoin sodium tablets marketed in India, on healthy Indian human volunteers

### Scientific Title of Study
Three way, three period, cross over bioequivalence study of single oral dose of three brands of 300mg Phenytoin sodium tablets marketed in India, on healthy Indian human volunteers

### Secondary IDs if Any

<table>
<thead>
<tr>
<th>Secondary ID</th>
<th>Identifier</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCP/KEM/Abbott/02</td>
<td>Protocol Number</td>
</tr>
</tbody>
</table>

### Details of Principal Investigator or overall Trial Coordinator (multi-center study)

<table>
<thead>
<tr>
<th>Name</th>
<th>Dr Mala DM Menon</th>
</tr>
</thead>
<tbody>
<tr>
<td>Designation</td>
<td>Professor of Pharmaceutics</td>
</tr>
<tr>
<td>Affiliation</td>
<td>Nil</td>
</tr>
<tr>
<td>Address</td>
<td>Bombay College of Pharmacy Kalina Santacruz East Mumbai 400098 India Nil Mumbai MAHARASHTRA 400098 India</td>
</tr>
<tr>
<td>Phone</td>
<td>02226670871</td>
</tr>
<tr>
<td>Fax</td>
<td>02226670816</td>
</tr>
<tr>
<td>Email</td>
<td><a href="mailto:maladmbcp@yahoo.co.in">maladmbcp@yahoo.co.in</a></td>
</tr>
</tbody>
</table>

### Details Contact Person (Scientific Query)

<table>
<thead>
<tr>
<th>Name</th>
<th>Dr Nithya Gogtay</th>
</tr>
</thead>
<tbody>
<tr>
<td>Designation</td>
<td>Associate professor</td>
</tr>
<tr>
<td>Affiliation</td>
<td>Nil</td>
</tr>
<tr>
<td>Address</td>
<td>Dept of clinical Pharmacology, Seth GS Medical college and KEM hospital Parel Mumbai 400012 India nil Mumbai MAHARASHTRA 400012 India</td>
</tr>
<tr>
<td>Phone</td>
<td>02224133767</td>
</tr>
<tr>
<td>Fax</td>
<td>02224112871</td>
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<tr>
<td>Email</td>
<td><a href="mailto:ngogtay@hotmail.com">ngogtay@hotmail.com</a></td>
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### Details Contact Person (Public Query)

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<tr>
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</table>
Source of Monetary or Material Support

Source of Monetary or Material Support

Primary Sponsor

Primary Sponsor Details

Name
Abbott India Limited

Address
Abbott India Limited Clinical Operations Sion Trombay Road 3-4 Corporate Park Mumbai Maharashtra 400071 India

Type of Sponsor
Pharmaceutical industry-Indian

Details of Secondary Sponsor

Name
NIL

Address
NIL

Countries of Recruitment

List of Countries
India

Sites of Study

Name of Principal Investigator
Dr Nithya Gogtay

Name of Site
Department of Clinical Pharmacology

Site Address
Dept of clinical Pharmacology, Seth GS Medical college and KEM hospital Parel Mumbai 400012 India

Phone/Fax/Email
02224133767 02224112871 njgogtay@hotmail.com

Details of Ethics Committee

Name of Committee
Ethics Committee for research on human subjects

Approval Status
Approved

Date of Approval
22/02/2010

Is Independent Ethics Committee?
No

Regulatory Clearance Status from DCGI

Status
Not Applicable

Date
No Date Specified

Health Condition / Problems Studied

Health Type
Healthy Human Volunteers

Condition
BA/BE study will be conducted in Normal healthy volunteer for epilepsy condition

Intervention / Comparator Agent

Type
Intervention

Name
Tablet Phenytoin Brand name: Eptoin

Details
one tablet contains 100 mg, total 3 tablets

Type
Comparator Agent

Name
Tablet Epsolin

Details
one tablet contains 100 mg, total 3 tablets

Type
Comparator Agent

Name
Tablet Celetoin

Details
one tablet contains 100 mg, total 3 tablets

Inclusion Criteria

Inclusion Criteria

Age From
18.00 Year(s)

Age To
45.00 Year(s)

Gender
Male

Details
Weight range within 20% of the ideal body weight as per standard tables and Indian criteria.
Age 18-45 years of male gender only.
Patients willing to sign informed consent form before undergoing screening.
Patients willing to undergo follow up for 2-6 months.
Physical examination: all findings of physical examination are normal with no ongoing serious illness that may affect the outcome of the study. Biochemical and hematologic test values (done within 2 week of the study), urine examination, and ECG all within normal limit. Negative for Hbs Ag (Australia antigen) and HIV. Agreement to abstain from caffeine on the day of the study and from alcohol and any other medication for 48 hours prior to entry into the study and during the course of the study

### Exclusion Criteria

<table>
<thead>
<tr>
<th>Details</th>
<th>Timepoints</th>
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<tbody>
<tr>
<td>History of intercurrent or concurrent diseases chronic alcohol consumption or drug addiction.</td>
<td>blood will be collected at 0,1,2,3,4,5,6,8,10,12,24,36,48,60 and 72 hours and parameters will be collected at these time points</td>
</tr>
<tr>
<td>History of chronic GI, renal, hepatic, cardiovascular, CNS, respiratory, infectious, or psychiatric diseases that affect the outcome of the study.</td>
<td></td>
</tr>
<tr>
<td>History of allergy or hypersensitivity to phenytoin sodium, consumption of tobacco in any form, participation in a new drug study in the past 6 months and in a bioavailability or any study of a marketed drug in the past 3 months, donating blood in the past 3 months, Any drug intake in the past 15 days or intake of an enzyme-inducing agent in the past 30 days.</td>
<td></td>
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### Method of Generating Random Sequence

Computer generated randomization

### Method of Concealment

Sequentially numbered, sealed, opaque envelopes

### Blinding/Masking

Participant, Investigator and Outcome Assessor Blinded

### Primary Outcome

To calculate pharmacokinetic parameters such as Cmax, tmax, AUC0-t and compare it with comparator drugs

### Secondary Outcome

nil

### Target Sample Size

Total Sample Size = 20
Sample Size from India = 20

### Phase of Trial

Phase 4

### Date of First Enrollment (India)

20/06/2011

### Date of First Enrollment (Global)

No Date Specified

### Estimated Duration of Trial

Years = 0
Months = 6
Days = 0

### Recruitment Status of Trial (Global)

Not Applicable

### Recruitment Status of Trial (India)

Completed

### Brief Summary

Most antiepileptic drugs (AEDs) have a narrow therapeutic index, and have a high potential for CNS-related adverse events, which is usually related to the serum concentration of the drug. There is no scientific evidence, as of now to predict that the 20% variability in bioavailability recommended...
by guidelines can be tolerated by patients with epilepsy. Dosage adjustment is required to provide optimal seizure control while avoiding adverse drug effects. The titration of dose of antiepileptic drugs is guided by target dose, plasma drug concentration reference range or seizure response. In the individual patient the range of effective and tolerable antiepileptic drug dose or plasma drug concentration is often not known. Management regimens may become very complex, with titration sometimes taking weeks in order to avoid adverse effects. Patients need their medication to be consistent during titration so that prescribed changes of dose have predictable consequences.

Phenytoin is poorly soluble in physiological fluids, and its bioavailability is therefore strongly influenced by various factors, particularly particle size and the substances used as excipients in the formulation. In designing formulations, there are three pharmacologic risk factors- low water solubility, a narrow therapeutic index and non-linear pharmacokinetics. Generic drugs contain the identical active ingredient(s) as the innovator medicine drug however the excipients (inactive ingredients) may vary. The rate and extent of absorption or bioavailability often differs between different generic versions of branded products, and each differs from the branded formulation itself, which can have serious effects for that patient. For example, a slight increase in phenytoin bioavailability can lead to a marked increase in serum level and thus to adverse effects, especially when the level is more than 15mg/L. Furthermore, nonlinear pharmacokinetics (e.g., phenytoin, PHT) and protein binding (e.g., valproate, VPA) can amplify even slight differences in bioavailability.

In India, there have been very limited studies in this direction. One study reported is comparison in the bioavailability of a single oral 200-mg dose of four brands of phenytoin sodium available in the Indian market; the results of the study revealed that one brand was bioinequivalent. Other comparisons indicate but do not prove bioinequivalence of the other brands. Study concludes that in India switching phenytoin brands could have significant implications and is not advisable once a patient is carefully titrated on one formulation.