PRODUCT SUMMARY

1. Trade name of the medicinal product

NORSK - NO DATA

2. Qualitative and quantitative composition

NORSK - NO DATA

3. Pharmaceutical form

NORSK - NO DATA

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

USES
ACTION:
MEXITIL IS AN ANTI-ARRHYTHMIC AGENT WHICH DEPRESSES THE MAXIUM RATE OF DEPOLARISATION WITH LITTLE OR NO MODIFICATION OF RESTING POTENTIALS OR THE DURATION OF ACTION POTENTIALS.
INDICATIONS:
FOR THE TREATMENT OF EXISTING OR ANTICIPATED VENTRICULAR ARRHYTHMIAS AND ECTOPIC BEATS SUCH AS THOSE FOUND AFTER MYOCARDIAL INFARCTION AND IN ISCHAEMIC HEART DISEASE.I.V MEXILETINE HAS BEEN USED SUCCESSFULLY IN THE TREATMENT OF VENTRICULAR ARRHTHMIAS INDUCED BY DIGITALIS.
MEXILETINE HAS ALSO BEEN PROVEN TO BE OF SOME BENE FIT IN IDIOPATHIE AND OTHER ARRHYTHMIC HAS ALSO BEEN PROVEN TO BE O F SOME BENEFIT IN IDIOPATHIC AND OTHER ARRHYTHMIC STATES.MEXILETINE IS O FTEN EFFECTIVE IN PATIENTS WITH GOOD LEFT VENTRICULAR FUNCTION,IN SUPPR ESSING VENTRICULAR ARRRHYTHMIAS REFRACTORY TO OTHER TREATMENT,MEXILETIN E IS NOT NOT OF PROVEN VALUE IN ARRHYTHMIAS IN PRE-EXCITATION SYNDROMES .

4.2 Posology and Method of Administration

DOSAGE AND ADMINSTRATION:
1.INTRAVENOUS MEXITIL:
A)LOADING DOSE:IV INJECTION OF 4-10ML(100-250MG)MEXITIL GIVEN AT A SUGGESTED RATE OF 1ML PER MINUTE(25MG PEER MINUTE)
THEN
ADD 500MG(2 AMPOULES)MEXITUIL TO 500ML OF A SUITABLE INFUSION SOLUTION(SEE PHARMACEUTICAL PRECAUTYIONS)ADMINSTER THE FIRST 250ML BY IV INFUSION OVER 1 HOUR(4ML PER MINUTE).
THEN ADMINSTER THE SECOND 250ML BY IV INFUSION OVER 2 HOURS(2ML PER MINUTE).
B)MAINTENANCE DOSE:ADD 250MG(1 AMPOULE)MEXITIL TO 500ML OF A SUITABLE INFUSION SOLUTION(SEE PHARMACEUTICAL PRECAUTIONS)ADMINSTER BY IV INFUSION AT A SUGGESTED RATE OF 1ML PER MINUTE(0.5 PER MINUTE),ACCORDING TO PATIENT RESPONSE.CONTINUE FOR AS LONG AS REQUIRED OR UNTIL ORAL MAINTENANCE THERAPY IS COMMENCED.
2.ORAL MEXITIL
A)LOADING DOSE:GIVE 400MG MEXITIL.
B)MAINTENANCE DOSE:GIVE 200-250 MG MEXITIUL THREE TO FOUR TIMES DAILY COMMENCING 2 HOURS AFTER THE LOADING DOSE.THE USUAL DAILY DOSE IS BETWEEN 600-800MG IN DIVIDED DOSES.
NOTE:MEXITIL IS ABSORBED IN THE UPPER PART OF THE SAMLL INTESTINE.
IN ACUTE MYOCARDIAL INFARCTION AND PARTICULARLY WHEN OPIATES HAVE BEEN

GIVEN RATE OF ABSORPTION BUT NOT BIOAVAILABILKITY MAY BE DELAYED AND THEREFORE A LARGER LOADING DOSE EG 600MG MAY BE PREFERABLE.
3.ALTERNATIVE LOADING DOSE REGIMES:
A)COMBINATION IV MEXITIL AND ORAL MEXITIL LOADING DOSE:IV INJECTION OF 8ML(200MG)MEXITUIL GIVEN AT A SUGGESTED RATE OF 1ML PER MINUTE.ON COMPLETION OF INJECTION OR INFUSION GIVE 400MG MEXITIL ORALLY.
MAINTENANCE DOSE
AS IN 2B
B)COMBINATION IV LIGNOCAINE AND ORAL MEXITIL LOADING DOSE:
GIVE IV LIGNOCAINE ACCORDING TO MANUFACTURE'S INSTRUCTIONS ON COMPLETION OF INJECTION GIVE 400MG MEXITIL ORALLY.
MAINTENANCE DOSE
AS IN 2B.
4.CHANGE OVER IV TO ORAL MEXITIL MAINTENANCE:
ON DISCONTINUING THE IV INFUSION COMMENCE THE MAINTENANCE DOSE.GIVE 200-250MG MEXITIL ORALLY THREE OR FOUR TIMES A DAY.
1.THE LOADING DOSE REGIME IS DESIGNED TO COMPENSATE FOR THE RAPID OF TISSUE DISTRIBUTION WHICH OCCURS ESPECIALLY WITH IV LOADING.
2.SIDE EFFECTS ARE MORE LIKELY TO BE ENCOUNTERED DURING THE INITIAL LOADING PHASE IN WHICH CASE THE RATE OF INFUSION SHOULD BE REDUCED.
3.IF THE OPTIMUM THERAPEUTIC EFFECT IS NOT ACHIEVED THE RATE OF INFUSION OR ORAL DOSAGE MAY BE INCREASED,SIDE EFFECTS PERMITTING.
4.GASTRIC EMPTYING TIME MAY BE DELAYED IN THE PATIENTS WITH MYOCARDIAL INFARCTION AND?OR TO WHOM OPAITES HAVE BEEN GIVEN AND THUS IT MATY BE NECESSARYU TO TITRATE THE DOSE AGAINST THERAPEUTIC EFFECTS AND SIDE EFFECTS.
FOR FURTHER DETAILS PLEASE REFER TO GOLD FILE.

4.3/4.9 Clinical particulars section

A) HYPERSENSITIVITY TO MEXILETINE, CARDIOGENIC SHOCK AND HIGH DEGREE A-V BLOCK UNLESS A PACEMAKER IS IN SITU.
B) INTERACTIONS WITH OTHER MEDICAMENTS AND OTHER FORMS OF INTERACTION:
(I) DRUGSS WHICH DELAY THE RATE OF ABSORPTION (NARCOTIC ANALGESICS, SOME ANTACIDS) MAY REDUCE PEAK PLASMA CONCENTRATION OF MEXILETINE.
(II) DRUGS WHICH INDUCE THE HEPATIC MIXED FUNCTION OXIDASE SYSTEM (E.G. RIFAMPICIN, PHENYTOIN AND PHENOBARBITOL) CAN INFLUENCE THE METABOLISM AND HENCE LOWER PLASMA LEVELS OF MEXILETINE.
(III) DRUGS WHICH ACIDIFY OR ALKALINISE URINE WILL ENHANCE OR REDUCE (RESPECTIVELY) THE RATE OF DRUG ELIMINATION.
(IV) THE PHARMACOKINETICS OF MEXILETINE ARE NOT SIGNIFICANTLY ALTERED BY WARFARIN, NITRAZEPAM, CIMETIDINE OR RANITIDINE.
(V) MEXITIL MAY BE USED CONCURRENTLY WITH THE CARDIOVASCULAR DRUGS DIGOXIN, AMIODARONE, QUINIDINE AND BETA-ADRENERGIC BLOCKING AGENTS. HOWEVER, CORCOMITANT I.V. THERAPY WITH OTHER LOCAL ANAESTHETIC-TYPE AGENTS SUCH AS LIGNOCAINE OR PROCAINAMIDE IS NOT RECOMMENDED, ALTHOUGH NO PROBLEMS HAVE BEEN ENCOUNTERED USING ORAL MEXILETINE IN CONJUNCTION WITH THESE DRUGS.
C) EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:
NONE KNOWN.
D) OTHER UNDESIRABLE EFFECTS (FREQUENCY AND SERIOUSNESS):
SIDE-EFFECTS: SIDE EFFECTS ARE MAINLY RELATED TO BLOOD CONCENTRATION AND MAY THEREFORE BE SEEN DURING THE INITIAL PHASES OF BOTH I.V. AND ORAL TREATMENT WHEN FLUCTUATION MAY OCCUR BEFORE THE BLOOD AND TISSUE CONCENTRATIONS REACH EQUILIBRIUM. REDUCING THE RATE OF INJECTION OF INFUSION OR DELAYING THE NEXT ORAL DOSE ALLOWS THE BLOOD CONCENTRATION TO FALL AND USUALLY REDUCES SIDE-EFFECTS. GENERALLY SIDE-EFFECTS ARE OF FOUR TYPES:
GASTROINTESTINAL - NAUSEA, VOMITING, INDIGESTION, UNPLEASANT TASTE, HICCOUGHS.

CENTRAL NERVOUS SYSTEM - LIGHT-HEADEDNESS, DROWSINESS, CONFUSION, DIZZINESS, DIPLOPIA, BLURRED VISION, NYSTAGMUS, DYSARTHRIA, ATAXIA, TREMOR, PARAESTHESIAE, CONVULSION, PSYCHIATRIC AND SLEEP DISORDERS. ANIMAL STUDIES USING TOXIC DOSES HAVE SHOWN THAT BENZODIAZEPINES (DIAZEPAM) REDUCE THE CNS EFFECTS.
CARDIOVASCULAR - HYPOTENSION, SINUS BRADYCARDIA, ATRIAL FIBRILLATION, PALPITATION, CONDJUCTION DEFECTS, EXACERBATION OF ARRHYTHMIAS AND TORSADE DE POINTES.
WHEN HYPOTENSION HAS OCCURRED THIS HAS TENDED TO BE IN PATIENTS WITH SEVERE ILLNESS WHO HAVE ALREADY BEEN GIVEN A VARIETY OF ANTI-ARRHYTHMIC OR OTHER PREPARATIONS AND, IF ASSOCIATED WITH BRADYCARDIA, MAY BE REDUCED BY THE USE OF ATROPINE.
HAEMATOLOGICAL- RASH, JAUNDICE.
E) USE IN PREGNANCY AND LACTATION:
ALTHOUGH MEXITIL HAS BEEN IN GENERAL USE FOR SEVERAL YEARS, THERE IS NO DEFINITE EVIDENCE OF SAFETY DURING HUMAN PREGNANCY. MEXILETINE FREELY CROSSES THE PLACENTA: HOWEVER, ANIMAL STUDIES HAVE SHOWN NO HAZARD.
AS WITH ALL MEDICINES, MEXILETINE SHOULD NOT BE USED IN PREGNANCY, ESPECIALLY THE FIRST TRIMESTER, UNLESS THE EXPECTED BENEFIT IS THOUGHT TO OUTWEIGH ANY POSSIBLE RISK TO THE FOETUS.
MEXILETINE IS SECRETED IN BREAST MILK (AT CONCENTRATIONS ON AVERAGE SLIGHTLY HIGHER THAN MATERNAL BLOOD), BUT HAS NOT BEEN DETECTED IN THE PLASMA OF THE SUCKLING INFANT. NEVERTHELESS CAUTION SHOULD BE EXERCISED , PARTICULARLY WHEN NURSING A PREMATURE INFANT.
F) OTHER SPECIAL WARNINGS AND PRECAUTIONS
WHEN MEXILETINE THERAPY IS COMMENCED, PATIENTS SHOULD BE MONITORED CLOSELY (ECG AND BLOOD PRESSURE, ROUTINE LABORATORY TESTS) PARTICULARLY IN THE FOLLOWING SITUATIONS:
SINUS NODE DYSFUNCTION, CONDUCTION DEFECT, BRADYCARDIA, HYPOTENSION OR CARDIAC, RENAL OR HEPATIC FAILURE. THERE MAY BE POTENTIATION OF TREMOR IN PATIENTS WITH PARKINSONISM.
THE DURATION OF TREATMENT REQUIRED IN ANY PATIENT IS OF NECESSITY VARIABLE, AND ALTHOUGH NO PRECISE GUIDE CAN BE GIVEN, WITHDRAWAL OF TREATMENT MAY BE ATTEMPTED AFTER A SUITABLE PERIOD FREE OF ARRHYTHMIA. GRADUAL WITHDRAWAL, I.E. OVER 1-2 WEEKS, IS PREFERABLE AS ARRHYTHMIAS WHICH HAVE BEEN SATISFACTORILY CONTROLLED MAY RECUR.
MYOCARDIAL INFARCTION RESULTS IN PROLONGED ABSORPTION HALF-LIFE OF MEXILETINE. PLASMA ELIMINATION HALF-LIFE MAY BE PROLONGED IN MODERATE TO SEVERE HEPATIC DISEASE, AND IN PATIENTS WITH CREATININE CLEARANCE OF LESS THAN 10 ML/MIN.
G) OVERDOSE (SYMPTOMS. EMERGENCY PROCEDURES, ANTIDOTES:
OVERDOSAGE: THE MINIMUM FATAL DOSE IS UNKNOWN BUT 4.40 G PROVED FATAL IN A HEALTHY YOUNG ADULT.
THE CLINICAL FEATURES INCLUDE NAUSEA, VOMITING, DROWSINESS, CONFUSION, ATAXIA AND CONVULSIONS. BLURRED VISION AND PARAESTHESIAE HAVE ALSO BEEN REPORTED. HYPOTENSION, SINUS BRADYCARDIA, ATRIAL FIBRILLATION AND CARDIAC ARREST ARE MORE SPECIFIC EFFECTS.
GASTRIC LAVAGE SHOULD BE PERFORMED WHEN APPROPRIATE AND THE PATIENT SHOULD BE TRANSFERRED (FOR FURTHER DETAILS SEE GOLD FILE).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

THE BASIC CELLULAR ELECTROPHYSIOLOGICAL EFFECT OF MEXILETINE IS A SLOWING OF THE MAXIMAL RATE OF DEPOLARIZATION OF THE ACTION POTENTIAL. IN PURKINJES FIBRES MEXILETINE DECREASES THE DURATION OF THE ACTION POTENTIAL.MEXILETINE BLOCKS SODIUM CHANNELS WITH A RAPID RATE OF ONSET AND RECOVERY.MEXILETINE MAY HAVE VAGOLYTIC ACTIVITY.
IN PATIENTS,MEXILETINE INCREASES THE FUNCTIONAL REFRACTORY PERIOD OF THE

ATRIO-VENTRAICULAR NODE AND ATRIO-VENTRICULAR CONDUCTION TIME AND SHIFTS THE WENCKEBACH POINT TO A LOWER RATE.MEXILETINE INCREASE THE RELATIVE AND EFFECTIVE REFRACTORY PERIODS OF THE HIS-PURKINJE SYSTEM.
REFERENCE:CAMPBELL,R.N.F.,N.E.J MEDICINE 316 29-34 (1987)

5.2 Pharmacokinetic properties

MEXILETINE IS PRIMARILY ABSORBED IN THE UPPER PORTION OF THE SMALL INTESTINE.PEAK PLASMA ARE REACHED 1.5 HOURS AFTER ADMINSTRATION TO NORMAL SUBJECTS;ABSORPTION IS SLOWER AFTER MYOCARDIAL INFARCTION. MEXILETINE SHOWS A FAST DISTRIBUTION PHASE,A SLOW DISTRIBUTION PHASE, AND A SLOW ELIMINATION PHASE.TISSUE UPTAKE IS SUBSTANTIAL.MEXILETINE UNDERGOES LESS THAN 10% FIRST PASS HEPATIC METABOLISM.BIOAVAILABILITY IS ABOUT 90%.RENAL CLEARANCE VARIES WITH URINE PH BUT THIS IS UNLIKELY TO HAVE CLINICAL SIGNIFICANCE.IN PATIENTS THE ELIMINATION HALF-LIFE IS 10-15 HOURS.
REFERENCE:CAMPBELL,R.N.F.,N.E.J.MEDICINE 316 29-34(1987)

PHARMACEUTICAL PROPERTIES

6.1 List of excipients

NORSK - NO DATA

6.2 Incompatibilites

NORSK - NO DATA

6.3 Shelf life

NORSK - NO DATA

6.4 Special precautions for storage

NORSK - NO DATA

6.5 Nature and contents of container

NORSK - NO DATA

6.6 Instructions for use/handling

NORSK - NO DATA

ADMINISTRATION DETAILS

7. Marketing authorization holder

NORSK - NO DATA

8. Marketing Authorization number

NORSK - NO DATA

9. Date of first authorization/renewal of authorization

NORSK - NO DATA

10. Date of (partial) revision of the text

NORSK - NO DATA