

Body As A Whole

Cardiovascular system

Digestive system

Hemic and lymphatic system

Anemia, ecchymosis, leukocytosis,
lymphadenopathy, polycythemia.

Metabolic and nutritional

Alkaline phosphatase increased,
hypercholesteremia,

Musculoskeletal system

Arthritis, arthrosis, , leg
cramps, myopathy

Nervous system

Agitation,
convulsion,

stupor.

Respiratory system

Apnea, epistaxis, hiccup,

Skin and appendages

Acne, alopecia,

rash,

Special senses

taste loss,

Urogenital system

albuminuria,

menorrhagia,

papanicolaou Papanicolau smear suspicious, polyuria, prostatic disorder, testis

urine frequency,

Review and Evaluation of Clinical Data

NDA (Serial Number)	21196 (000)
Sponsor:	Orphan Medical, Inc.
Drug:	Xyrem
Proposed Indication:	Narcolepsy
Material Submitted:	Labeling Review
Correspondence Date:	9/30/00
Date Received / Agency:	10/3/00
Date Review Completed	6/14/01
Reviewer:	Ranjit B. Mani, M.D.

Background

This submission contains an original New Drug Application for Xyrem® (sodium oxybate; γ-hydroxybutyrate) oral solution.

This document reviews the sponsor's proposed labeling as proposed in the original application and as modified in a further submission dated 12/16/00.

The safety and efficacy data in this application have each been reviewed by me in separate applications.

The sponsor's draft labeling, as edited by me, is presented below. My editing and review of the label have been confined to sections subsumed under my clinical reviews

Edited Draft Labeling

Draft Professional Insert (December 15, 2000 Version) Modified to include information from Trial OMC-SXB-21 and OMC-SXB-20

R_x only

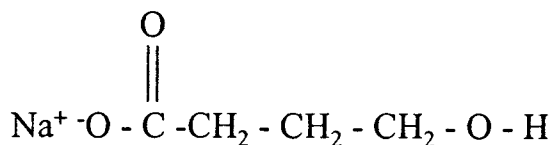
CIII

Xyrem® (sodium oxybate) oral solution

DESCRIPTION

Xyrem (sodium oxybate) is a neuroactive agent with effects on sleep architecture that include increased slow wave sleep, increased delta power, and decreased

nocturnal awakenings. Xyrem is intended for oral administration. The chemical name for sodium oxybate is gamma-hydroxybutyric acid (GHB), sodium. The molecular formula is $\text{NaC}_4\text{H}_7\text{O}_3$ and the molecular weight is 126.1 grams/mole. The chemical structure is:



Sodium oxybate is a white to off-white, crystalline powder that is very soluble in aqueous solutions. Xyrem contains 500 mg of sodium oxybate per milliliter of USP purified water, neutralized to pH 7.5 with malic acid.

CLINICAL PHARMACOLOGY

Mechanism of Action

Pharmacokinetics and Metabolism

Absorption

is absorbed following oral administration. The average peak plasma concentration

Administration of after a high fat meal resulted in average T_{max} increasing from 0.75 hr to 2.0 hr and reductions in peak plasma levels (C_{max}) of 58% and systemic exposure (AUC) by 37%.

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