INTRODUCTION TO PATIENT-REPORTED OUTCOMES (PROs) SUCH AS HEALTH-RELATED QUALITY OF LIFE, TREATMENT SATISFACTION, ETC

Stockholm

Thursday, March 4

13:15-14:45

Regulatory Issues

EMEA and the Regulatory Environment

Labels in Europe?

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Four Examples with PRO label

« New » Products (2001-2003)

- PRO primary Outcome
  - BEXTRA, EBIXA, VESICARE
- PRO secondary Outcome
  - AERIUS

Community register of medicinal products for human use

Bextra

Alphabetical list Chronological list

INN :
Valdecoxib
Indication:
Symptomatic relief in the treatment of osteoarthritis or rheumatoid arthritis.

Treatment of primary dysmenorrhoea
Marketing Authorisation Holder:
Pharmacia-Pfizer EEIG

	da	de	el	en	es	fi	fr	it	nl	pt	sv	Decision date of last change
Product characteristics	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	27 Mar 2003
Marketing Authorisation Holder	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	27 Mar 2003
Labelling	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	27 Mar 2003
Package Leaflet	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	27 Mar 2003

EU Number	Presentation	Authorisation date
EU/1/02/239/001	Bextra - 10 mg - Film - coated tablets - Oral use - Blister (PVC/alu) - 5 tablets	27 Mar 2003

5.1 Pharmacodynamic properties

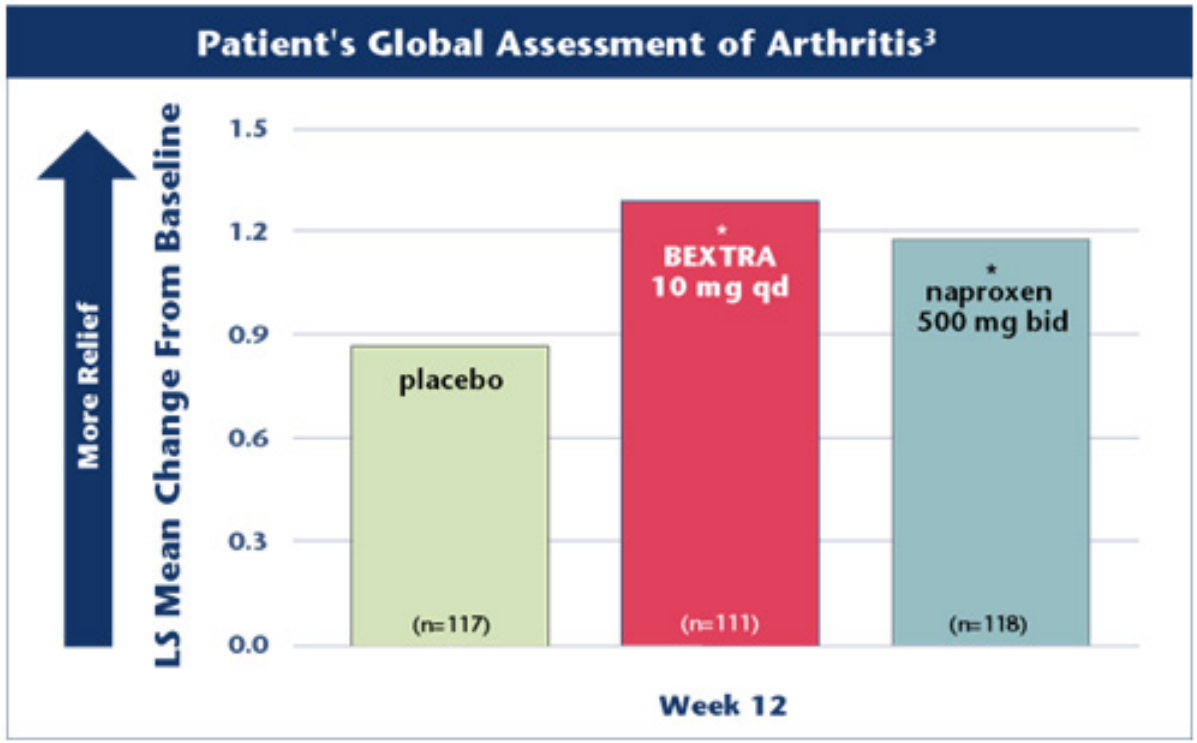
Osteoarthritis: Valdecoxib was evaluated in six double-blind, randomised controlled trials in which approximately 2670 patients with osteoarthritis were treated for 6 to 52 weeks.

Valdecoxib 10 mg and 20 mg once daily **demonstrated significant improvement compared to placebo and was similar to naproxen 500 mg twice daily in a composite assessment of pain, stiffness and physical function measures** in two 12-week studies of patients with osteoarthritis of the hip or knee, and relief of arthritis pain was reported within 24 hours of the first dose.

In a 26 week study in patients with osteoarthritis of the knee or hip (some of whom also had osteoarthritis of the hand and/or spine), valdecoxib 10 mg and 20 mg once daily was shown to be clinically comparable to diclofenac 75 mg twice daily.

Study of OA of the knee[4]

Study design:
Randomized, multicenter, double-blind, placebo-controlled, 12-week comparison study (N=466) of the efficacy and safety of BEXTRA 5 mg. qd, 10 mg. qd, and naproxen 500 mg. bid in patients with OA of the hip.



- **Patient's Global Assessment of Arthritis was a primary efficacy evaluation.**
  The scale ranged from 1 ("very good") to 5 ("very poor").
  Assessments were performed at weeks 2, 6, and 12.

- **Baseline value: 4.1 for all treatment groups.**[3]

*Both treatment groups significantly better vs placebo (P<0.04).[3]
BEXTRA was not significantly different vs naproxen.[3]

Community register of medicinal products for human use

Ebixa

Alphabetical list Chronological list

INN :
Memantine
Indication:
Treatment of patients with moderately severe to severe Alzheimer's disease
Marketing Authorisation Holder:
H. Lundbeck A/S

	da	de	el	en	es	fi	fr	it	nl	pt	sv	Decision date of last change
Product characteristics	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	20 Nov 2002
Marketing Authorisation Holder	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	15 May 2002
Labelling	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	27 Sep 2002
Package Leaflet	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	20 Nov 2002

EU Number	Presentation	Authorisation date
	COUNTRIES APPLICATION DATE EU MARKETING AUTHORISATION NATIONAL PROCEDURES MARKETING DATE	
EU/1/02/219/001	Ebixa - 10 mg - Film-coated tablets - Oral use - Blister (Alu/PP) - 30 tablets	15 May 2002

5.1 Pharmacodynamic properties

Patients with moderate-to-severe Alzheimer's disease were randomly assigned to receive placebo or 20 mg of **memantine** daily for 28 weeks.

The primary efficacy variables were the Clinician's Interview-Based Impression of Change Plus Caregiver Input (CIBIC-Plus) and **the Alzheimer's Disease Cooperative Study Activities of Daily Living Inventory modified for severe dementia (ADCS-ADLsev).**

The secondary efficacy end points included the Severe Impairment Battery and other measures of cognition, function, and behavior.

Lundbeck Ebixa memantine

5.1 Pharmacodynamic properties

Treatment differences between base line and the end point were assessed.

Missing observations were imputed by using the most recent previous observation (the last observation carried forward). The results were also analyzed with only the observed values included, without replacing the missing values (observed-cases analysis).

Results Two hundred fifty-two patients (67 percent women; mean age, 76 years) were enrolled. Of these, 181 (72 percent) completed the study and were evaluated at week 28. Seventy-one patients discontinued treatment prematurely (42 taking placebo and 29 taking **memantine**).

5.1 Pharmacodynamic properties

Patients receiving **memantine** had a better outcome than those receiving placebo, according to the results of:

- the CIBIC-Plus (P=0.06 with the last observation carried forward, P=0.03 for observed cases),
- the ADCS-ADLsev (P=0.02 with the last observation carried forward, P=0.003 for observed cases), and
- the Severe Impairment Battery (P<0.001 with the last observation carried forward, P=0.002 for observed cases).

Memantine was not associated with a significant frequency of adverse events

Ebixa – Efficacy in key areas

Ebixa provides:

- **an improvement in function, cognition and global response**
- **advantages in self--care and general functioning in everyday life leading to an improvement in both patients ' and caregivers 'quality of life**
- proven efficacy up to 12 months
- a new opportunity to treat even severe AD with clinically relevant results

Community register of medicinal products for human use

Aerius

Chronological list

INN :
Desloratadine
Indication:
Symptoms associated with seasonal allergic rhinitis
Marketing Authorisation Holder:
Schering Plough Europe

	da	de	el	en	es	fi	fr	it	nl	pt	sv	Decision date of last change
Product characteristics	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	17 Mar 2003
Marketing Authorisation Holder	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	30 Sep 2002
Labelling	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	16 Apr 2002
Package Leaflet	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	17 Mar 2003

EU Number	Presentation	Authorisation date
EU/1/00/160/001	Aerius - desloratadine - 5mg - Film-coated tablet - Oral use - 1 tablet	15 Jan 2001
EU/1/00/160/002	Aerius - desloratadine - 5mg - Film-coated tablet - Oral use - 2 tablets	15 Jan 2001

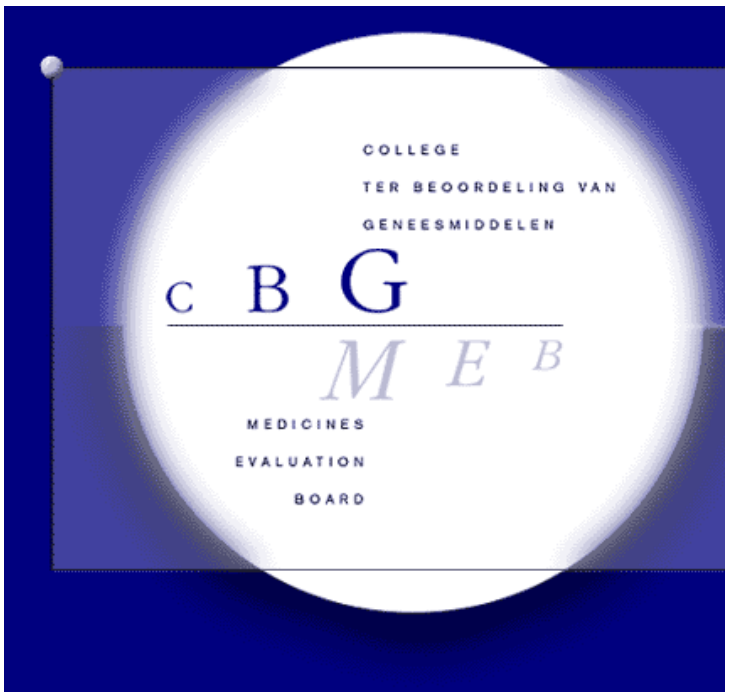
AERIUS
desloratadine

5.1 Pharmacodynamic properties

Aerius was effective in alleviating the burden of seasonal allergic rhinitis (SAR) as shown by the total score of the rhino-conjunctivitis quality of life questionnaire.

The greatest amelioration was seen in the domains of practical problems and daily activities limited by symptoms.

VESICARE® (solifenacin succinate)



The Netherlands (Reference Member State)

Approved in Dec 10th 2003

On-going Mutual Recognition

VESICARE® (solifenacin succinate)

5.1. Pharmacodynamic Properties

Pharmacodynamic effects

Treatment with Vesicare administered at dosages of 5 and 10 mg once daily has been investigated in a number of double-blind, randomized, controlled clinical studies in male and female patients with symptoms of an overactive bladder.

Compared with placebo, once daily administration of 5 and 10 mg Vesicare produced a statistically significant improvement in the overactive-bladder symptoms at all times (see table). The effect of the treatment is discernible after 1 week and stabilizes over a period of 12 weeks. A long-term open-label study showed that the effect is maintained for at least 12 months. After 12 weeks' treatment, approximately 50% of the patients with incontinence before treatment were continent and approximately 35% of the patients achieved a frequency of micturition of less than 8 times per day.

5.1. Pharmacodynamic Properties

Pharmacodynamic effects (continued)

Vesicare also brought about an improvement in a number of quality-of-life aspects, such as general perception of health, the effect of incontinence on quality of life, job restrictions, physical restrictions, social restrictions, emotions, severity of symptoms, measures related to the severity and the sleep/energy ratio.