

# CELEBREX<sup>TM</sup>

## *Description*

- CELEBREX (celecoxib) is chemically designated as 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl] benzenesulfonamide
- The empirical formula for celecoxib is  $C_{17}H_{14}F_3N_3O_2S$ , and the molecular weight is 381.38.
- CELEBREX oral capsules contain 100 mg and 200 mg of celecoxib.

# CELEBREX<sup>TM</sup>

## *Clinical Pharmacology*

- A nonsteroidal anti-inflammatory drug that exhibits anti-inflammatory, analgesic, and antipyretic activities in animal models.
- The mechanism of action is believed to be inhibition of prostaglandin synthesis, via inhibition of cyclooxygenase-2 (COX-2).
- Does not inhibit the cyclooxygenase-1 (COX-1) isoenzyme.

# CELEBREX<sup>TM</sup>

## *Pharmacokinetics*

- Peak plasma levels of celecoxib occur approximately 3 hrs after an oral dose.
- Highly protein bound (~97%) within the clinical dose range.
- Metabolism is primarily mediated via cytochrome P450 2C9
- Eliminated predominantly by hepatic metabolism with little (<3%) unchanged drug recovered in the urine and feces

# CELEBREX™

## *Pharmacokinetics*

- **Summary of Single Dose (200 mg) Disposition Kinetics in Healthy Subjects<sup>1</sup>**

- Mean (%CV) PK Parameter Values

<b>C<sub>max</sub></b>	<b>T<sub>max</sub></b>	<b>Effective t<sub>1/2</sub></b>	<b>V<sub>SS</sub>/F</b>	<b>CL/F</b>
<b>ng/mL</b>	<b>hr</b>	<b>hr</b>	<b>L</b>	<b>L/hr</b>
705 (38)	2.8 (37)	11.2 (31)	429 (34)	27.7 (28)

- <sup>1</sup>Subjects under fasting conditions (n=36, 19-52 yrs.)

# CELEBREX<sup>TM</sup>

## *Special Populations*

- Geriatric: Elderly subjects (over 65 y.o.) had a 40% higher C<sub>max</sub> and a 50% higher AUC.
- Pediatric: Has not been investigated in patients below 18 years of age.
- Race: Meta-analysis has suggested a 40% higher AUC in Blacks compared to Caucasians.
- Hepatic Insufficiency: In mild and moderate (Child's Class I & II) hepatic impairment AUC is increased 40% and 180%, respectively.
- Renal Insufficiency: No relationship was found between GFR and clearance.

# CELEBREX™

## *Drug Interactions*

- Significant interactions may occur when administered with drugs that inhibit P450 2C9.
- Celecoxib is not an inhibitor of cytochrome P450 2C9, 2C19 or 3A4.
- Clinical studies have identified potential interactions with fluconazole and lithium.
- Experience with NSAIDs suggests potential for interactions with furosemide and ACE inhibitors.
- No interactions with glyburide, ketoconazole, methotrexate, phenytoin, and tolbutamide

# CELEBREX<sup>TM</sup>

## *Clinical Studies*

- Osteoarthritis (OA): Significant reduction in joint pain when compared to placebo.
- Rheumatoid Arthritis (RA): Significant reduction in joint tenderness/pain and joint swelling when compared to placebo.
- Familial Adenomatous Polyposis (FAP): Shown to reduce the number of adenomatous colorectal polyps.

# CELEBREX™

## *Special Studies*

- Incidence of Gastroduodenal Ulcers from Endoscopic Studies in OA and RA Patients
- 3 Month Studies      Study 1 (n=1108)      Study 2(n=1049)

Placebo	2.3%(5/217)	2.0%(4/200)
Cele 50 mg BID	3.4% (8/233)	-----
Cele 100 mg BID	3.1%(7/227)	4.0% (9/223)
Cele 200 mg BID	5.9% (13/221)	2.7% (6/219)
Cele 400 mg BID	-----	4.1% (8/197)
Napr 500 mg BID	16.2% (34/210)*	17.6% (37/210)
- \*\*p ≤ 0.05 vs all other treatments, Cele = Celebrex, Napr = Naproxen

# CELEBREX™

## *Special Studies*

- Incidence of Gastroduodenal Ulcers from 3-Month Serial Endoscopy Studies in OA and RA Patients

• Study 3 (n=523)	Week 4	Week 8	Week 12	Final
Celebrex				
200 mg	4.0%	2.2%	1.5%	7.5%
BID	(10/252)*	(5/227)*	(3/196)*	(20/266)*
• Naproxen				
500 mg	19.0%	14.2%	9.9%	34.6%
BID	(47/247)	(26/182)	(14/141)	(89/257)

- \*p <= 0.05 Celebrex vs. naproxen based on interval and cumulative analyses

# CELEBREX™

## *Special Studies*

- Incidence of Gastroduodenal Ulcers from 3-Month Serial Endoscopy Studies in OA and RA Patients

• Study 4 (n=1062)	Week 4	Week 8	Week 12	Final
Celebrex	3.9%	2.4%	1.8%	7.0%
200 mg	(13/337)	(7/296)	(5/274)	(25/356)
BID	*	*	*	*
Diclofenac	5.1%	3.3%	2.9%	9.7%
75 mg	(18/350)	(10/306)	(8/278)	(36/372)
BID				
Ibuprofen	13.0%	6.2%	9.6%	23.3%
800 mg	(42/323)	(15/241)	(21/219)	(78/334)
TID				

- \*p <= 0.05 Celebrex vs. ibuprofen based on interval and cumulative analyses

# CELEBREX<sup>TM</sup>

## *Special Studies*

- Platelets: In clinical trials, CELEBREX at single doses up to 800 mg and multiple doses of 600 mg BID for up to 7 days duration (higher than recommended therapeutic doses) had no effect on platelet aggregation and bleeding time. Comparators (naproxen 500 mg BID, ibuprofen 800 mg TID, diclofenac 75 mg BID) significantly reduced platelet aggregation and prolonged bleeding time.

# CELEBREX<sup>TM</sup>

## *Indications and Usage*

- CELEBREX is indicated:
- 1) For relief of the signs and symptoms of osteoarthritis.
- 2) For relief of the signs and symptoms of rheumatoid arthritis in adults.
- 3) To reduce the number of adenomatous colorectal polyps in familial adenomatous polyposis (FAP), as an adjunct to usual care (e.g., endoscopic surveillance, surgery).

# CELEBREX™

## *Contraindications*

- Patients with known hypersensitivity to celecoxib.
- Patients who have demonstrated allergic-type reactions to sulfonamides.
- Patients who have experienced asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAIDs. Severe, rarely fatal, anaphylactic-like reactions to NSAIDs have been reported in such patients