

Date: July 19, 2007

Subject: DRC Recommendations to DCC and DHS

To: DHS, DCC, Dean's Office

From: Henry F. Simmons, Jr., MD, Ph.D.
Chairman DRC

At its 07/19/07 meeting, the Drug Review Committee considered the potential toxicity and therapeutic roles of selected calcium channel blockers and targeted immune modulators.

PART I

Calcium channel blockers under consideration include the following:

Phenylalkylamine

Verapamil

Benzothiazepine

Diltiazem

Dihydropyridine

Amlodipine

Felodipine

Isradipine

Nicardipine

Nifedipine

Nisoldipine

Indications under consideration in adults

Angina

Systolic dysfunction [LVEF<45%]

Supraventricular dysrhythmias

Essential hypertension [BP \geq 140/90]

Conclusions regarding calcium channel blockers

1. None of the available calcium channel blockers is associated with clinically evident adverse events of sufficient severity or number to exclude it from further consideration.
2. The three classes of calcium channel blockers in use differ pharmacologically to the degree that at least one representative of each should be accessible to prescribers. Accordingly, verapamil, diltiazem and at least one dihydropyridine should be available.
3. When considering use of the dihydropyridines for the captioned indications, the Committee reached the same conclusions as its predecessor in 2005 with the following exception: Amlodipine and at least one other dihydropyridine should be available. The reaffirmed 2005 recommendations follow.

That amlodipine, nicardipine, nifedipine and nisoldipine are considerations for patients with angina

That amlodipine, isradipine, nicardipine, nifedipine and nisoldipine are considerations for patients with hypertension

That amlodipine be available to patients in the following categories:

- Patients with both angina and documented left ventricular systolic dysfunction

- Patients with hypertension and documented left ventricular systolic dysfunction

- Patients with angina, hypertension, and documented left ventricular systolic dysfunction

4. None of the captioned drugs have been proven to differ significantly in either the incidence or nature of clinically evident adverse effects in patients of a particular demographic group.

5. None of the captioned drugs have been proven more efficacious for patients of a particular demographic group.

PART II

Targeted immune modulators under consideration

Abatacept (Orenicia)

Adalimumab (Humira)

Alefacept (Amevive)

Anakinra (Kineret)

Efalizumab (Raptiva)

Etanercept (Enbrel)

Infliximab (Remicade)

Rituximab (Rituxan)

Indications under consideration in adults

Rheumatoid arthritis

Ankylosing spondylitis

Psoriatic arthritis

Crohn's disease

Ulcerative colitis

Plaque psoriasis

Indications under consideration in children

Juvenile rheumatoid arthritis

Conclusions regarding targeted immune modulators

There is insufficient evidence to conclude that one of the available agents differs from the others in terms of safety considerations or frequency of adverse events to the degree that it should be stricken from further consideration.

In the treatment of **rheumatoid arthritis** there is sufficient information to conclude that Orenicia (abatacept), Humira (adalimumab), Kineret (anakinra), Enbrel (etanercept) and Remicade (infliximab) and Rituxan (rituximab) are efficacious for the treatment of rheumatoid arthritis in adults. However, Kineret (anakinra) is not as efficacious as adalimumab (Humira), etanercept (Enbrel) and rituximab (Rituxan). At least two of the FDA approved agents should be available, in particular if Kineret (anakinra) is one of them.

Humira (adalimumab), Enbrel (etanercept) and Remicade (infliximab) efficacious for treatment of **ankylosing spondylitis**. At least two of these FDA approved agents should be available.

For the treatment of **psoriatic arthritis** at least two of the following should be available: Humira (adalimumab), Enbrel (etanercept) and Remicade (infliximab).

For the treatment of **Crohn's disease** either Humira (adalimumab) or Remicade should be available.

Remicade (infliximab) should be available for the treatment of **ulcerative colitis**.

At least two of the following agents should be available for the treatment of **plaque psoriasis**: alefacept (Amevive), efalizumab (Raptiva), etanercept (Enbrel) and infliximab (Remicade).

In the treatment of **juvenile rheumatoid arthritis**, Enbrel (etanercept) should be available.

With respect to use of the aforementioned immune modulators among individuals from different demographic groups there is insufficient data to conclude that one is either more efficacious or more likely to produce adverse events than another.

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