**Darunavir boosted with ritonavir (DRV/r)**

3rd line drug information for the Clinician

**Class:** HIV-1 Protease inhibitor (PI)

**Dose:**

1. Adults: Darunavir 600 mg (1 tablet) + Ritonavir 100 mg (1 tablet) bd p.o. with food

2. Children:

3-18 years of age (>10kg): DRV 20 mg/kg bd p.o.

**\*\*\*Not Recommended in Pediatric Patients below 3 Years of Age\*\*\***

**Side effects:**

**Most common adverse effects:** headache, nausea, diarrhea, amylase elevations, rash

**Most significant adverse effects:**

**-**Drug induced Hepatotoxicity in 0.5%, caution and possibly monitor LFTs in patients with Hepatitis B and C infection, cirrhosis. In severe chronic liver disease DRV/r is not recommended.

**-**Severe Skin and Hypersensitivity Reactionsin 0.4%, (potentially life-threatening/ fatal) Stevens-Johnson syndrome, Toxic epidermal necrolysis,

-Hypersensitivity reactions = rash + constitutional findings (fever, general malaise, fatigue, muscle/joint aches, blisters, oral lesions, conjunctivitis, facial edema, hepatitis, eosinophilia, angioedema).

- DRV/R has a sulphur component, so use careful if at all in patients with sulphur allergy.

- Like other protease inhibitors (LPV/r, ATV/r) it can cause metabolic changes like diabetes mellitus (New onset DM and exacerbation of pre-existing DM), hyperglycemia and fat redistribution (central obesity, buffalo hump, peripheral wasting, facial wasting, breast enlargement, and “cushing appearance”)

**Drug-Drug Interactions:**

DRV/R will interact with other drugs, elevated plasma concentrations are associated with serious and/or life-threatening events, some drugs may increase or reduce levels of DRV:

1. ***TB treatment: rifampicin results in significant decrease in plasma concentrations of darunavir, resulting in loss of therapeutic effect and development of resistance. DRV/r can not be combined with TB treatment.***
2. Phosphodiesterase inhibitors e.g. sildenafil or Viagra**®**, tadalafil
3. Statins e.g. simvastatin and lovastatin
4. Benzodiazepines e.g. midazolam
5. Ergotamine (migraine treatment)
6. Some herbal Medicines

Potential Important Drug-Drug Interactions with DRV/RTV:

|  |  |
| --- | --- |
| Drug name (Drug class) | Effect |
| Antiarrhythmics:  e.g. amiodarone, lidocaine, digoxin | ↑ levels of Antiarrhythmic |
| Clarithromycin | ↑ levels |
| Warfarin | ↓ levels |
| Anticonvulsants:  carbamazepine  phenobarbitone, phenytoin | ↔ darunavir  ↑ carbamazepine  ↔ darunavir  ↓ phenytoin  ↓ phenobarbital |
| Antidepressants:  Selective Serotonin Reuptake  Inhibitors (SSRIs):  paroxetine, sertraline  Tricyclic Antidepressants (TCAs):  amitriptyline, | ↓ paroxetine  ↓ sertraline  ↑ amitriptyline |
| Antimalarial:  artemether/lumefantrine | ↓ artemether  ↓ dihydroartemisinin  ↑ lumefantrine (risk of QT prolongation)  ↔ darunavir |
| Antineoplastics e.g. vincristine | ↑ Antineoplastics |
| B-blockers and calcium channel blockers | ↑ levels (closely monitor pts, consider dose reduction of the B-blocker and CCB) |
| Corticosteroids (systemic/inhaled/nasal) | ↑ levels |
| Oral Contraceptive pill | ↓ levels, use additional methods eg condoms |
| Benzodiazepines/Sedatives/hypnotics: eg diazepam, IV midazolam | ↑ levels |

NOTE: No dosage adjustments are recommended when DRV/R is co-administered with the

following medications: NRTIs (abacavir, emtricitabine, lamivudine, stavudine, tenofovir, zidovudine), raltegravir, ranitidine.

If you need to co-prescribe any other drugs with DRV/R, check for potential for dangerous interactions on the following website: <http://www.hiv-druginteractions.org/> or the British National Formularly or contact the Pharmacovigilance centre at College of Medicine.

Discourage patients from using herbal medicines or drugs bought on the streets and at the market.

WRITTEN INFORMATION TO BE GIVEN TO THE PATIENT

**DARUNAVIR WITH RITONAVIR**

This is a combined pill used in combination with other pills to suppress HIV. It stops the virus from multiplying by blocking one of its enzymes called protease.

\*Take 1 tablet (600mg) TWICE daily TAKEN WITH FOOD

If you are allergic to sulphur containing medicines such as cotrimoxazole (bactrim), tell your doctor, you may not be prescribed darunavir which is also a sulphur containing medicine (depending on how severe your previous reaction was).

Some common side effects of darunavir may include diarrhoea; nausea, rash, stomach pain, and vomiting. These will improve over days or weeks.

Report to your clinic if you develop rash that may include sores in the eyes, mouth and on the skin with fever; yellowing of eyes and muscle pains.

Report to your clinic if you develop yellowing of eyes that may be accompanied by stomach pains with or without stomach tenderness (to the right side), nausea and vomiting. Your medicine may need to be stopped.

Report to your clinic if you experience anything else that you think may be related to your taking this medicine.

Darunavir may affect the way your liver works especially the way it removes from the body poisons and medicines we take. It is very important that you take medicines and vitamins prescribed by the doctors and nurses in your clinic. Do not take herbal medicines or medicines sold on the streets or at the market while you are taking Darunavir.