

Cystic Fibrosis (CF) Modulator Therapies

Why are you receiving this briefing?

- This briefing has been authored as there has been a reported increase in incidents where patients with CF, who are prescribed modulator therapies have been prescribed other medicines that interact with their modulator therapies.
- This means there is specific drug groups that shouldn't be co-administered or require dose adjustment.
- Commonly affected drugs are:
 - Clarithromycin
 - Fluconazole
 - Oral hormonal contraceptives

What is Cystic Fibrosis (CF)

- Cystic Fibrosis (CF) is caused by a faulty gene that affects the production of a protein called CFTR. Its production is affected by different mutations. There are over 2000 known mutations that can cause CF.
- The gene affected by CF controls the movement of salt and water in and out of cells. People with CF experience a build-up of thick sticky mucus in the lungs, digestive system, and other organs, causing a wide range of challenging symptoms affecting the entire body.

CF Modulator therapies

- CF modulators are life-saving drugs that work to tackle the underlying cause of Cystic Fibrosis, the treatment depends on the mutation.
- Modulators currently available in England are:
 - Ivacaftor (Kalydeco®)
 - Lumacaftor with ivacaftor (Orkambi®)
 - Tezacaftor with ivacaftor (Symkevi®)
 - Ivacaftor with elexacaftor and tezacaftor (Kaftrio®)
- Children and young people with CF, who are eligible to be prescribed modulator therapies, will have them prescribed by their specialist CF team and often have them delivered directly to their home.

Actions

- **It is important when prescribing or dispensing other medications alongside modulators, to be aware of potential drug to drug interactions.**
 - Follow this link - [Clinical impact of CFTR modulator therapy roll-out - The Pharmaceutical Journal](#).
- The table overleaf summarises dose adjustments and drugs which are not advised for co-administration.
- If you spot a potential problem/incorrect dose, contact the prescriber.
- If you have further questions, contact the patients CF Specialist team for further advice. The patient or their care giver will be able to advise who their CF team is and provide contact details.

	Ivacaftor (Kalydeco®)	Lumacaftor with ivacaftor (Orkambi®)	Tezacaftor with ivacaftor (Symkevi®)	Elexacaftor with ivacaftor and tezacaftor (Kaftrio®)
Weak or moderate CYP3A inhibitors (e.g. fluconazole, isavuconazole, erythromycin)	-One ivacaftor tablet every morning; -No tablet in the evening.	-No dose adjustment of Orkambi required but higher dose of CYP3A inhibitor may be required to obtain desired clinical effect. -Ideally use alternative	-Alternate one Symkevi tablet and one Ivacaftor tablet every morning; -No tablet in the evening.	-Alternate two Kaftrio tablet and one ivacaftor tablet every morning; -No tablet in the evening.
Strong CYP3A Inhibitors (e.g. itraconazole, posaconazole, voriconazole and clarithromycin)	-One ivacaftor tablet twice a week (taken approximately three to four days apart); -No tablet in the evening.	-No dose adjustment of Orkambi required but higher dose of CYP3A inhibitor may be required to obtain desired effect. -Ideally use alternative. -Concomitant use with Posaconazole is not recommended.	-One Symkevi tablet twice a week (taken approximately three of four days apart); -No tablet in the evening.	-Two Kaftrio tablets twice a week (taken approximately three to four days apart); -No tablet in the evening.
Strong CYP3A inducer (e.g. rifampicin, rifabutin, phenytoin and St John's wort)	Co-administration with strong CYP3A inducers is not recommended. Use alternatives			
Hormonal contraception	Ivacaftor is not expected to modify the efficacy of the hormonal contraceptives.	Hormonal contraceptives, including oral, injectable, transdermal, and implantable should not be relied upon as an effective method of contraception when co-administered with Orkambi.	Symkevi and ivacaftor are not expected to modify the efficacy of hormonal contraceptives.	Kaftrio is not expected to modify the efficacy of hormonal contraceptives. For patients taking hormonal contraceptives who develop rash, interrupting treatment with Kaftrio and hormonal contraceptives should be considered.