Chemotherapy Protocol

Breast Cancer

Abemaciclib-Fulvestrant

Regimen

- Breast Cancer – Abemaciclib-Fulvestrant

Indication

- Abemaciclib in combination with fulvestrant is indicated for the treatment of hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer where the following criteria have been met;

  - the patient has histologically or cytologically documented oestrogen receptor positive and HER-2 negative breast cancer
  - the patient has metastatic breast cancer or locally advanced breast cancer which is not amenable to curative treatment
  - the patient is male or is female and if female is either post-menopausal or if pre- or peri-menopausal has undergone ovarian ablation or suppression with LHRH agonist treatment
  - the patient has received previous endocrine therapy according to one of the three populations as set out below as these are the only groups for which there was evidence submitted to NICE for the use of abemaciclib plus fulvestrant. The populations are has progressive disease whilst still receiving adjuvant or neoadjuvant endocrine therapy for early breast cancer with no subsequent endocrine therapy received following disease progression **or** has progressive disease within 12 or less months of completing adjuvant endocrine therapy for early breast cancer with no subsequent endocrine therapy received following disease progression **or** has progressive disease on 1st line endocrine therapy for advanced/metastatic breast cancer with no subsequent endocrine therapy received following disease progression
  - the patient has had no prior treatment with a CDK 4/6 inhibitor unless abemaciclib has been received as part of any compassionate use scheme for the combination of abemaciclib plus fulvestrant and the patient meets all the other criteria set out here
  - the patient has had no prior treatment with fulvestrant
  - the patient has had no prior treatment with everolimus
  - treatment will continue until there is progressive disease or excessive toxicity or until the patient chooses to discontinue treatment, whichever is the sooner
  - treatment breaks of up to 6 weeks are allowed, but solely to allow toxicities to settle
  - WHO performance status of 0, 1, 2

Toxicity

Treatment breaks of up to 6 weeks are allowed but solely to allow toxicities to settle.

Drug	Adverse Effect
Abemaciclib	Infection, myelosuppression, peripheral neuropathy, fatigue, mucositis, anorexia, eye disorders, venous thromboembolism, diarrhoea, raised liver enzymes
Fulvestrant	Osteoporosis, headache, somnolence, hot flushes, alopecia, arthralgia, rash, vaginal dryness, asthenia, liver abnormalities, depression, insomnia, injection site reactions, nausea

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

Drugs

- FBC, LFTs and U&Es at baseline and then every two weeks for the first eight weeks. (a four week supply may be dispensed on day 1 of each cycle even though monitoring may be every two weeks). The frequency of monitoring can then reduce to once every four weeks for a further eight weeks and then as indicated (patients should be assessed every 12 weeks as a minimum).

Dose Modifications

The dose modifications listed are for haematological, liver and renal function only. Dose adjustments may be necessary for other toxicities as well.

In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.

Please discuss all dose reductions / delays with the relevant consultant before prescribing if appropriate. The approach may be different depending on the clinical circumstances. The following is a general guide only.

Haematological

Dose modifications for haematological toxicity in the table below are for general guidance only. Always refer to the responsible consultant as any dose reductions or delays will be dependent on clinical circumstances and treatment intent.

Consider blood transfusion or the use of erythropoietin according to NICE TA323 if patient symptomatic of anaemia or has haemoglobin of less than 8g/dL (80g/L)

Prior to prescribing cycle 1 the following criteria must be met.

Criteria	Eligible Level
Neutrophils	Equal to or more than $1.5x10^9$/L
Platelets	Equal to or more than $100x10^9$/L

No dose reductions are required for fulvestrant due to myelosuppression. For abemaciclib, dose adjustments for haematological toxicity are described in the table below;

Abemaciclib Dose Adjustments	
Recommended dose	150 mg twice daily
First dose adjustment	100 mg twice daily
Second dose adjustment	50 mg twice daily

Doses of abemaciclib should be adjusted as follows for haematological toxicity.

Toxicity (NCI CTC)	Management Recommendations
Grade 1 or 2	No dose adjustment required.
Grade 3	Suspend dose until toxicity resolves to NCI grade 2 or less. Dose reduction is not required.
Grade 3, recurrent; or grade 4	Suspend dose until toxicity resolves to NCI grade 2 or less. Resume at next lower dose.
Patient requires administration of blood cell growth factors	Suspend abemaciclib dose for at least 48 hours after the last dose of blood cell growth factors was administered and until toxicity resolves to NCI grade 2 or less. Resume at next lower dose unless the dose was already reduced for the toxicity that led to the use of the growth factor.

Hepatic Impairment

No dose change for fulvestrant is recommended in patients with mild hepatic disease. Caution is advised in patients with moderate to severe hepatic impairment

Alanine aminotransferase (ALT) and aspartate aminostransferase (AST) should be monitored prior to the start of abemaciclib therapy, every two weeks for the first two months, monthly for the next two months, and as clinically indicated.

Toxicity (NCI CTC)	Management Recommendations (Abemaciclib)
Grade 1 or 2	No dose adjustment required.
Persistent or recurrent grade 2 or grade 3	Suspend dose until toxicity resolves to baseline or Grade 1. Resume at next lower dose.
Grade 4	Discontinue abemaciclib.

Renal Impairment

No dose change is recommended for fulvestrant in patients with mild or moderate renal impairment. In patients with severe renal impairment, administration of fulvestrant should be performed with caution

No dose adjustments for abemaciclib are necessary in patients with mild or moderate renal impairment. There are no data regarding abemaciclib administration in patients with severe renal impairment, end stage renal disease, or in patients on dialysis. Abemaciclib should be administered with caution in patients with severe renal impairment, with close monitoring for signs of toxicity.

Other

Abemaciclib

Diarrhoea

Treatment with antidiarrhoeal agents, such as loperamide, should be started at the first sign of loose stools.

Diarrhoea	Management Recommendations (Abemaciclib)
Grade 1	No dose adjustment required.
Grade 2	If toxicity does not resolve within 24 hours to Grade 1 or less, suspend dose until resolution. Dose reduction is not required.
Grade 2 that persists or recurs after resuming the same dose despite maximal supportive measures	Suspend dose until toxicity resolves to Grade 1 or less. Resume at next lower dose.
Grade 3 or 4 or requires hospitalisation	

Other toxicities should be managed as follows;

Toxicity (not haematology or diarrhoea or liver)	Management Recommendations (Abemaciclib)
Grade 1 or 2	No dose adjustment required.
Persistent or recurrent grade 2 toxicity that does not resolve with maximal supportive measures to baseline or Grade 1 within 7 days	Suspend dose until toxicity resolves to grade 1 or less. Resume at next lower dose.
Grade 3 or 4	

Regimen

28 day cycle until disease progression or intolerance (twelve cycles will be set in ARIA)

Ovarian ablation or suppression with a LHRH agonist is mandatory is patients who are pre or peri menopausal due to the pharmacology of palbociclib and aromatase inhibitors in combination. This is not included in the regimen on ARIA.

Cycle One

Drug	Dose	Days	Route
Abemaciclib	150mg twice a day	Days 1-28 inclusive	Oral
Fulvestrant	500mg	1 and 15	Intramuscular

Cycle Two onwards

Drug	Dose	Days	Route
Abemaciclib	150mg twice a day	Days 1-28 inclusive	Oral
Fulvestrant	500mg	1	Intramuscular

Fulvestrant will be set up to be administered in the hospital setting (internal). If it is to be dispensed by the hospital and administered elsewhere please change this to a pickup internal in ARIA.

Dose Information

- Abemaciclib is available as 150mg, 100mg and 50mg film coated tablets

Administration Information

- If the patient vomits or misses a dose of abemaciclib, an additional dose should not be taken that day. The next prescribed dose should be taken at the usual time

- Fulvestrant should be administered as two consecutive 5 ml injections by slow intramuscular injection (1-2 minutes/injection), one in each buttock (gluteal area).Caution should be taken if injecting fulvestrant at the dorsogluteal site due to the proximity of the underlying sciatic nerve.

Supportive Treatments

- Loperamide 4mg after the first loose stool and 2mg after each subsequent loose stool to a maximum of 16mg in 24 hours

Additional Information

- The National Patient Safety Alert on oral chemotherapy (NPSA/2008/RRR001) must be followed in relation to abemaciclib

- It must be made clear to all staff, including those in the community, that abemaciclib should only be prescribed under the supervision of a consultant oncologist

- Abemaciclib interacts with many other agents, especially those that affect CYP 3A4. Always check for drug interactions.

- Ovarian ablation or suppression with a LHRH agonist is mandatory is patients who are pre or peri menopausal due to the pharmacology of abemaciclib and aromatase inhibitors in combination.

- Treatment breaks of up to 6 weeks are allowed but solely to allow toxicities to settle

Coding

- Procurement - X
- Delivery – X

References

1.

REGIMEN SUMMARY

Abemaciclib-Fulvestrant

Cycle One

Day One

1. Abemaciclib 150mg twice a day for 28 days oral
   Administration Instructions
   Oral chemotherapy

2. Fulvestrant 500mg intramuscular
   Administration Instructions
   Fulvestrant should be administered as two consecutive 5 ml injections by slow intramuscular injection (1-2 minutes/injection), one in each buttock (gluteal area).Caution should be taken if injecting fulvestrant at the dorsogluteal site due to the proximity of the underlying sciatic nerve. Please refer to the package insert for instructions on administering the injection

Day Fifteen

3. Fulvestrant 500mg intramuscular
   Administration Instructions
   Fulvestrant should be administered as two consecutive 5 ml injections by slow intramuscular injection (1-2 minutes/injection), one in each buttock (gluteal area).Caution should be taken if injecting fulvestrant at the dorsogluteal site due to the proximity of the underlying sciatic nerve. Please refer to the package insert for instructions on administering the injection

Take Home Medicines (day one only)

4. Loperamide 4mg after the first loose stool and 2mg after each subsequent loose stool to a maximum of 16mg in 24 hours
   Administration Instructions
   Take 4mg after the first loose stool and then 2mg after each subsequent loose stool to a maximum of 16mg in 24 hours. Please supply one original pack size

Cycle Two Onwards

Day One

5. Abemaciclib 150mg twice a day for 28 days oral
   Administration Instructions
   Oral chemotherapy

6. Fulvestrant 500mg intramuscular
   Administration Instructions
   Fulvestrant should be administered as two consecutive 5 ml injections by slow intramuscular injection (1-2 minutes/injection), one in each buttock (gluteal area).Caution should be taken if injecting fulvestrant at the dorsogluteal site due to the proximity of the underlying sciatic nerve. Please refer to the package insert for instructions on administering the injection

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	June 2019	None	Dr Deborah Wright Pharmacist	Dr Sanjay Raj Consultant Medical Oncologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury Hospital NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors which occur as a result of following these guidelines.