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NICE Health Technology Appraisal

Appraisal of oxaliplatin and capecitabine for the adjuvant treatment of colorectal cancer

External submission on behalf of
British Oncology Pharmacy Association
April 2005

Capecitabine

The British Oncology Pharmacy Association welcomes the inclusion of this technology review in that it will provide an oral choice for patients who currently have to accept intravenous therapy. In assessing its impact on the NHS cancer services under the heading of **'cost effectiveness and the wider implications for the NHS'**, it will be necessary to compare capecitabine against the five 5-fluorouracil/folinic acid (5FU/FA) schedules currently used in the UK to treat colorectal cancer in the adjuvant setting. There are significant differences between the five schedules, in terms of drug cost, cost of disposables and type of venous access required. There is also considerable variation in the burden to the patient, nursing service and pharmacy service. This submission will focus on the pharmacy service.

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Summary of commonly used 5FU schedules

Regimen	**Modified de Gramont** (MdG) (12 cycles over 6 months)	**De Gramont** (dG)	**MAYO** Days 1-5 q 4-5 weeks X6	**Weekly 5FU/FA** (30 weeks)	**Continuous 5FU infusion** (6 months)
Schedule	5FU 300mg/m^2 5FU 2400mg/m^2 FA 175mg/m^2	5FU 300mg/m^2 X2 5FU 1200mg/m^2 X2 FA 175mg/m^2	5FU 425mg/m^2 FA 20mg/m^2	5FU 350mg/m^2 FA 30mg	300mg/m^2 continuously for 6 months
Drug Costs including disposables £(estimate)	2153	1961	300	270	762
Estimated time to make/ course (minutes)	900	720	450	450	720

The figures shown in the table are estimates based on the chemotherapy reference costs and preparation times calculated for hospitals within the Peninsula Cancer Network. As was demonstrated from the reference costs submitted nationally in 2004, these will vary considerably between hospitals. However, it would be generally accepted that infusional 5FU schedules are more labour intensive and expensive than those using bolus administration only. De Gramont and modified de Gramont schedules use high dose FA which is more expensive than the lower dose equivalent. Generally the FA for all schedules would be drawn up by nurses in the clinical area. This would reflect a burden on nursing time, but not pharmacy time.

Dose banding is a widely used technique which has successfully contributed to the semi-automation of bolus 5FU dispensing (Pharm.J (270) p691-5 17 May 2003). Consequently, this line of therapy is not one of the greatest burdens to chemotherapy units. Dose banding is not applied as frequently to the infusional schedules, although many chemotherapy providers now source 5FU-containing cassettes/reservoirs for infusional therapies from external providers. Where this is the case, the differential workload impact of the various schedules is minimised but the cost differentials are *increased.*

Capecitabine dispensing is undertaken in the main dispensary area in most hospitals. A capecitabine prescription would not be viewed as a straightforward prescription to dispense. There are two different tablet strengths, 150mg and 500mg. For an average patient receiving the usual dose of 1250mg/m^2 twice a day for 14 days, calculating quantities of each of the different tablet strengths needed; labelling and dispensing the tablets, is a complex process. A single cycle of capecitabine therapy involving 14 days drug treatment may require as many as 252 tablets. These would usually be dispensed by non-specialist pharmacy staff. A tablet counting check would

be advised in addition to the routine prescription check due to the toxic nature of the drug and the consequences of giving the wrong number of tablets. For such a drug, where the dose (in terms of the number of tablets of each strength) is customised for every patient, clear, concise, consistent and unambiguous labelling is of paramount importance. The risks associated with dispensing oral cancer drugs have been discussed in a position statement produced by our organisation (www.bopa-web.org and attached). Dispensing a capecitabine prescription would take at least 15 minutes per patient However; if capecitabine became mainline therapy in adjuvant colorectal cancer, systems could be developed to streamline the dispensing process and dose banding could be applied to facilitate this.

In summary;

BOPA would support this technology from the point of view of patient quality of life. It will clearly represent a reduction of workload in pharmacy chemotherapy units, but it *increases* the volume of complex dispensing work going through already overstretched dispensaries and transfers risk-management responsibilities to non-specialist staff. Since this dispensing process is likely to be replacing a process, which in the bolus 5FU setting, is largely automated, we would therefore view the net impact on pharmacy services as neutral i.e. a transfer, rather that a reduction, of workload. Moreover it is a change for which revised and customised systems of work and a different departmental infrastructure are likely to be warranted.

For cancer services currently using the dG and MdG schedules routinely, substitution of capecitabine should result in a net time- saving for pharmacy services However; it is our impression that in the UK, these 5FU schedules are only infrequently used in the adjuvant setting. In particular, it should be noted that we *strongly* recommend that all oral chemotherapy prescriptions be checked by specialist cancer pharmacists in the same way as prescriptions for i.v. treatment. This requires either the presence of one or more specialist pharmacists in the dispensary or direction of these prescriptions to the chemotherapy unit or a convenient area nearby i.e. redesign of current systems of work.

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Oxaliplatin

BOPA would support the inclusion of this technology for review on the clinical grounds that the evidence shows that adjuvant therapy may provide benefit to a group of good performance status patients with colorectal cancer. However there are issues we consider to be important in the assessment of this drug that would come under the headings of **cost effectiveness and wider implications to the NHS**

The paper from which the most impressive evidence is derived (MOSAIC;J Clin. Oncol. 2003;21:2896-2903) compares the De Gramont (dG) schedule alone with the combination of oxaliplatin and deG. If oxaliplatin is considered as an addition to routine adjuvant 5FU/FA chemotherapy in a proportion of colorectal cancer patients, this will constitute additional work for pharmacy chemotherapy units. If patients who would have otherwise routinely received bolus 5FU/FA therapy are now prescribed deG in combination with Oxaliplatin (following the MOSAIC trial exactly); this will constitute a still greater amount of extra work. (Please see preparation times tabled above)

Oxaliplatin Preparation

There are several reasons why oxaliplatin would be considered a time intensive and capacity absorbing drug for pharmacy services. They are as follow

- Expensive
- Short expiry once reconstituted
- No current potential for dose banding
- Reasonably toxic
- Fairly time consuming to make (about 45 minutes per infusion)

Combined with the cost, the risk of waste restricts the opportunity for preparation in advance If the treatment did not go ahead, the drug would almost certainly be wasted (potential for redeployment to another patient would be limited). Most pharmacy chemotherapy units would therefore either require the attendance of a patient at a pre-chemotherapy clinic or confirmation of the patient's arrival in the chemotherapy department and their readiness to go ahead with treatment before starting to prepare the dose. This could mean that a patient who would previously (for 5FU only) have attended the clinic once may have to attend twice; or, for same day treatment, the patient may be subjected to a long wait before the oxaliplatin can be started.

In Summary

Whist oxaliplatin may represent a therapeutic advance in the adjuvant treatment of some colorectal cancer patients, adopting this technology as an addition to 5FU/FA regimens currently used in the UK will create further capacity pressures within pharmacy and the clinical area.

Dr Libby Hardy
Lead Pharmacist
Peninsula Cancer Network

On behalf of
British Oncology Pharmacy Association