National Cancer Control Programme

NCCP Technology Review Committee (TRC)

Meeting Notes

Date of Meeting:	**27th January 2025 at 4.30pm**
Venue:	**Teleconference via MS Teams**
Assessment:	Fruquintinib (Fruzaqla®)
	Olaparib (Lynparza®)
	Pemigatinib (Innovent®)

TEXT FOR REDACTION DUE TO DELIBERATIVE PROCESS HIGHLIGHTED IN YELLOW

TEXT FOR REDACTION DUE TO COMMERCIAL SENSITIVITY IS HIGHLIGHTED IN PINK

TEXT FOR REDACTION DUE TO CONFIDENTIALITY IS HIGHLIGHTED IN BLUE

Attendance:

Members present		
NCPE representative	National Centre for Pharmacoeconomics (NCPE)	By MS Teams
Dr Neil Barrett	Consultant Haematologist, Children's Health Ireland - Crumlin	By MS Teams
Dr Patrick Hayden	Consultant Haematologist, St James's :IHS representative	By MS Teams
Ms Aishling McLoughlin	Chief I Pharmacist, NCCP (Chair)	By MS Teams
Ms Fiona Mulligan	PCRS representative	By MS Teams
Dr Adrian Murphy	Medical Oncologist, Beaumont: ISMO nominee	By MS Teams
Dr Susan Spillane	HTA Directorate: HIQA nominee	By MS Teams
Non-member invited specialists present		

Apologies (members)	
Dr Oscar Breathnach	Medical Oncologist, Beaumont: ISMO nominee
Dr Dearbhaile Collins	Consultant Medical Oncologist, Cork University Hospital: ISMO nominee
Dr Dearbhaile O'Donnell	Medical Oncologist, St. James's Hospital: ISMO nominee
Prof Michael O'Dwyer	Consultant Haematologist, Galway :IHS representative
Dr Susan Spillane	HTA Directorate: HIQA nominee
Observers present	
Ms Helena Desmond	Senior Pharmacist, NCCP — By MS Teams

Item	Discussion	Actions
1	**Introduction & reminder re. conflict of interest & confidentiality**	
	Members were reminded to raise any conflicts of interest that they had in relation to any drug for discussion prior to the commencement of the discussion of that item.	
2	**Notes of previous meeting and matters arising**	
	The notes of the previous meeting on December 2nd 2024 were reviewed, following an amendment the notes were and agreed.	
3	**Drugs/Technologies for consideration**	
	Fruquintinib (Fruzaqla®) (**Ref. TRC 165)** *As monotherapy is indicated for the treatment of adult patients with metastatic colorectal cancer (mCRC) who have been previously treated with available standard therapies, including fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapies, anti-VEGF agents, and anti-EGFR agents, and who have progressed on or are intolerant to treatment with either trifluridine-tipiracil or regorafenib.* The clinical aspects of this indication were discussed. Fruquintinib is an oral angiogenesis inhibitor indicated for the fourth line treatment of metastatic colorectal cancer (mCRC). The supporting evidence for this indication comes from the FRESCO-2 trial, a phase III, double-blind, placebo-controlled trial in patients with mCRC who had been previously treated with standard approved therapies including fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy; an anti-VEGF biological therapy; an anti-EGFR therapy if RAS wild-type, and have progressed on or had intolerance to trifluridine/tipiracil and/or regorafenib. The primary endpoint was overall survival (OS), and the trial demonstrated an improvement with fruquintinib compared to placebo with an OS of 7.4 months versus 4.8 months and HR of 0.66. The trial also showed an improvement in progression free survival (PFS) of 3.7 months with fruquintinib compared to 1.8 months with placebo. The safety profile was discussed, the safety reported in the FRESCO-2 trial was that expected for angiogenesis inhibitors, such as hypertension, hand foot syndrome for example, it was noted that higher adverse events were reported in the fruquintinib group compared to the placebo group, however clinicians noted that these side effects are manageable. It was also highlighted that fruquintinib is more selective in terms of angiogenesis signalling and it may be better tolerated than the comparator regorafenib. There is a desire among the clinicians to have fruquintinib available for this small. The pharmacoeconomic aspects as outlined in the rapid review (RR) assessment carried out by the NCPE were discussed, noting that a full HTA was recommended, but not completed. The relevant comparators, and the positioning of fruquintinib in the treatment pathway was outlined. The supporting evidence was discussed, noting that while the results for OS and PFS were small, given that fruquintinib is indicated for fourth line treatment the results are considered clinically and significantly longer compared to patients in the placebo group. In terms of the cost, based on a median treatment course of 3.1 months, the cost is estimated to be [redacted] compared to [redacted]. In terms of the budget impact (BI), it is estimated that [redacted] patients will be treated in year-1, increasing to [redacted] in year-5. Treatment with fruquintinib is associated with a gross BI of [redacted] over 5 years and a net BI of [redacted]. It was noted that a PAS offer has been submitted and negotiations are ongoing. Having considered the clinical efficacy of the indication in this patient cohort the committee members agreed unanimously to recommend approval of this indication to the HSE Drugs Group. *(Decision: TRC 165)* Olaparib (Lynparza®) (**Ref. TRC 166)** *As monotherapy for the maintenance treatment of adult patients with*	

	germline BRCA1/2-mutations who have metastatic adenocarcinoma of the pancreas and have not progressed after a minimum of 16 weeks of platinum treatment within a first-line chemotherapy regimen. The clinical aspects of this indication were discussed, noting that olaparib is well known for the treatment of *BRCA* mutated cancers, predominately in ovarian, breast and increasingly in prostate cancer. The supporting evidence for this indication is the POLO study, a phase III, randomised, double-blind, placebo-controlled study which investigated the use of olaparib for the maintenance treatment of adult patients with germline BRCA1/2-mutations who have metastatic adenocarcinoma of the pancreas and have not progressed after a minimum of 16 weeks of platinum treatment within a first-line chemotherapy regimen. The primary endpoint was progression free survival (PFS) by blinded independent central review (BICR), and the study showed an improvement in PFS of 7.4 months in the olaparib arm compared to 3.8 months in the placebo arm, the second PFS was 13.2 months versus 9.2 months in difference favouring olaparib. Overall survival (OS) was not significantly improved either numerically or statistically and showed an OS of 18.9 months in the olaparib arm compared to 18.1 months in the placebo arm, however the study was not powered for OS. It was noted that a large proportion of patients in the placebo group (87%) received subsequent treatment compared to the olaparib arm and duration of follow up was considerably shorter in the placebo arm. The safety profile was discussed, noting that olaparib is well known through its use in other tumours such as ovarian, breast and prostate, and clinicians are familiar with its known side effect profile, such as fatigue, anaemia for example. It was highlighted that olaparib is associated with adverse events of special interest, such as MDS and AML, a class effect of PARP, however none of these were reported in the POLO study. In terms of the prevalence it is estimated that 2% of patients with pancreatic cancer carry the *BRCA2* mutation and 1% carry *BRCA1* mutation, however, this is likely to be an over estimation. There is a desire among the clinicians to have olaparib available for this patient cohort, noting that the patient numbers will be low. The pharmacoeconomic aspects as outlined in the rapid review (RR) assessment carried out by the NCPE were discussed, noting that a full HTA was recommended, but not completed. The supporting clinical evidence was discussed. The NCPE Review Group highlighted a number of concerns and limitations regarding the supporting clinical evidence, such as subsequent treatment received, duration of follow up in the placebo group and patient population. The review group also raised concerns with the efficacy outcomes, noting that the trial was underpowered to detect any difference in OS which is the most relevant endpoint. In terms of the cost, the cost per treatment course was based on the median treatment duration and was estimated to be [redacted]. In terms of the budget impact (BI) the Applicant assumes that *BRCA* testing would be performed in [redacted] The NCPE review group considered this to be underestimation, It was noted that based on UK data, the Applicant assumes 4.6 % of pancreatic patients harbour a germline *BRCA* mutation, therefore leading to uncertainty. In terms of the budget impact (BI), the NCPE estimate that [redacted]. The gross BI estimated by the NCPE [redacted] over 5 years. When the cost of *BRCA* testing is considered (at a [redacted]) it is assumed that [redacted] and the net BI is estimated to be [redacted]. It was noted that there is a PAS in place for olaparib which would reduce the net drug BI.The NCPE recommended a full HTA based on the proposed price and given the limitation of the clinical efficacy data, lack of OS benefit and high cost of olaparib. Having considered the clinical efficacy of the indication in this patient cohort the committee members agreed by majority not recommend approval of this indication to the HSE Drugs Group. *(Decision: TRC 166)*	

Pemigatinib (Innovent®) **(Ref. TRC 167)**

As monotherapy for the treatment of adults with locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or rearrangement that is relapsed or refractory after at least one line of systemic therapy.

The clinical aspects of this indication were discussed. The supporting evidence for this indication comes from the FIGHT-202 trial, a phase II, open-label, single-arm, study which investigated the use of pemigatinib in the treatment of adult patients with locally advanced or metastatic cholangiocarcinoma with a *FGFR2* fusion or rearrangement who have progressed after at least one prior line of systemic therapy. The trial consisted of 3 cohorts, depending on *FGFR* status, with cohort A consisting of patients with *FGFR2* fusion or rearrangement, the population of relevance to this indication. *FGFR2* fusion or rearrangement affect 10-15% of patients with cholangiocarcinoma. The primary endpoint of the FIGHT-202 trial was objective response rate (ORR) and showed that treatment with pemigatinib resulted in an ORR of 37% with a 7 month progression free survival (PFS) and a median overall survival (OS) of 17.5 months. For comparative purposes pemigatinib is compared to second line chemotherapy options such as FOLFOX and FOLFIRI which typically have an ORR of 12% compared to 37%. The safety profile was discussed, the safety reported in the FIGHT-202 trial were expected for this class of drug, such as hyperphosphataemia (usually managed with dietary modifications), stomatitis and hand foot syndrome for example. It was highlighted that testing is required to identify eligible patients and approximately 200 patients with cholangiocarcinoma are diagnosed per year in Ireland, of those 10-15% will harbour the *FGFR2* fusion or rearrangement. There is a desire among the clinicians to have pemigatinib available for this niche patient population, noting a substantial benefit is expected for those who respond, while for non-responders, it is anticipated that treatment would be stopped after 3 months.

The pharmacoeconomic aspects as outlined in the rapid review (RR) assessment carried out by the NCPE were discussed, noting that a full HTA was recommended, however a HTA was not submitted. The supporting clinical evidence was discussed, concerns were raised regarding the magnitude of benefit, single arm nature of the trial and the uncertainty of the comparative efficacy evidence and relative effectiveness of pemigatinib. In terms of the cost, the cost per treatment course was based on treatment duration of 7.2 months and was estimated to [redacted] In terms of the budget impact (BI), it is assumed that [redacted] of those tested, it is estimated that 8.6% would have a *FGFR2* fusion or rearrangement, it is assumed that 60% of these would receive second line treatment. It is estimated that [redacted] The total treated population is estimated to [redacted] over 5 years. However clinical opinion obtained by the Applicant suggests this is underestimated and there is uncertainty regarding the number of patients that will be tested. The gross BI estimated to be [redacted]. There is potential cost off sets due to pemigatinib being an oral agent, for example the cost of IV administration and day ward attendance, however the testing cost are to be considered. Due to the uncertainly regarding the patient estimates, the NCPE review group performed a scenario analysis increasing the estimated number of patients treated from [redacted] over 5 years, which increased the cumulative 5-year gross BI to [redacted] including VAT. The NCPE recommended a full HTA based on the proposed price, and given, lack of lack comparative efficacy evidence the relative effectiveness of pemigatinib being highly uncertain. It was also noted by the NCPE review group that a full HTA would not resolve the uncertainty regarding the comparative effectiveness.

	Having considered the clinical efficacy of the indication in this patient cohort the committee members agreed unanimously to recommend approval of this indication to the HSE Drugs Group subject to an improvement in cost *(Decision: TRC 167)*	
4	**Update on other drugs in the reimbursement process**	
	An update had been shared with the group in the documentation for the meeting	
5	**Next meeting**	
	The proposed date for the next meeting is February 24th 2025	
6	**Any other business / Next meeting**	

The meeting concluded at 17.50pm.

Actions arising from meeting:

Ref.	Date of meeting	Details of action	Responsible	Update
25/01	27/01/2025	NCCP to communicate recommendations to HSE Drugs Group.	NCCP	Complete
25/01	27/01/2025	Apply for CPD	NCCP	Complete