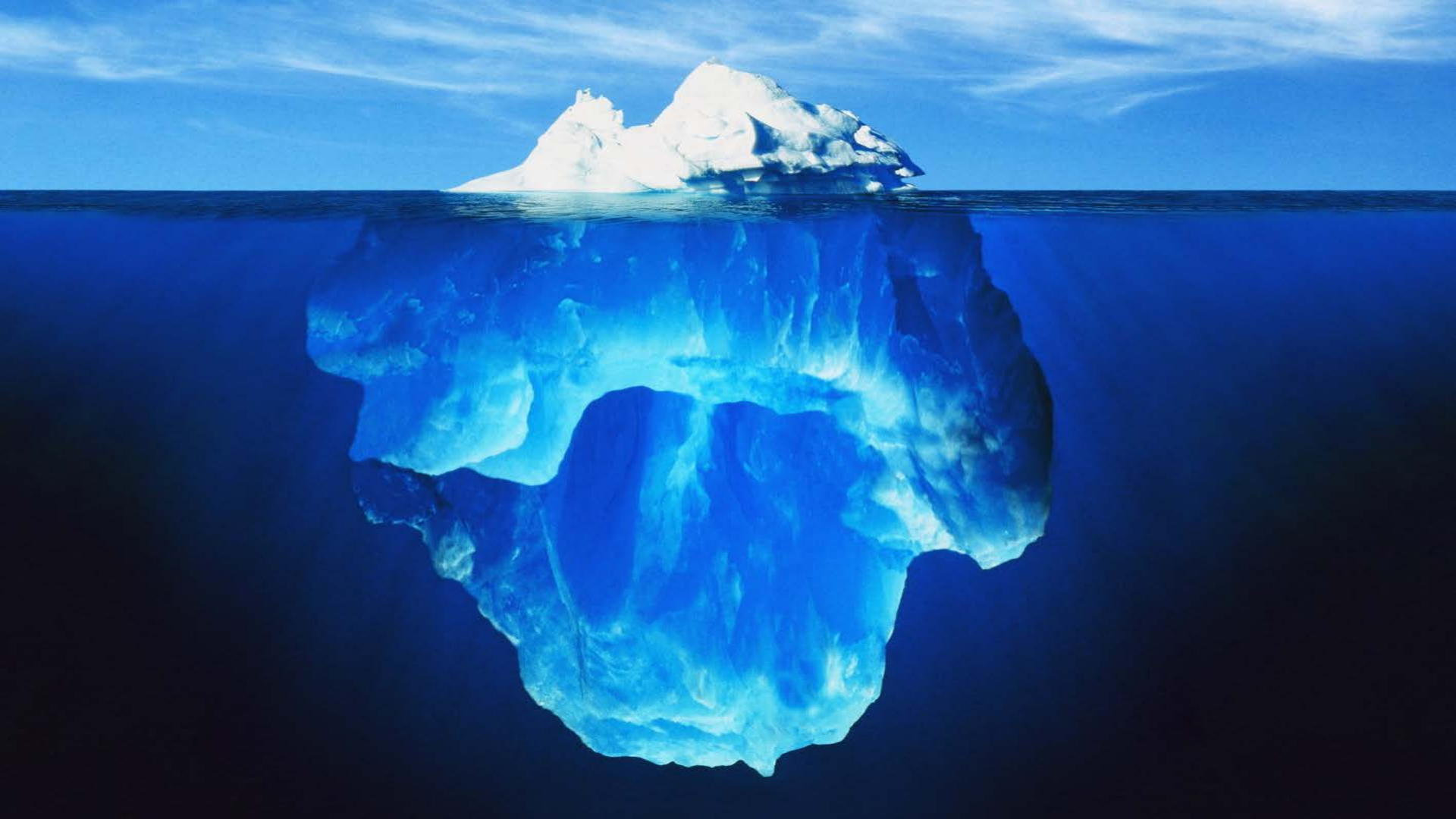
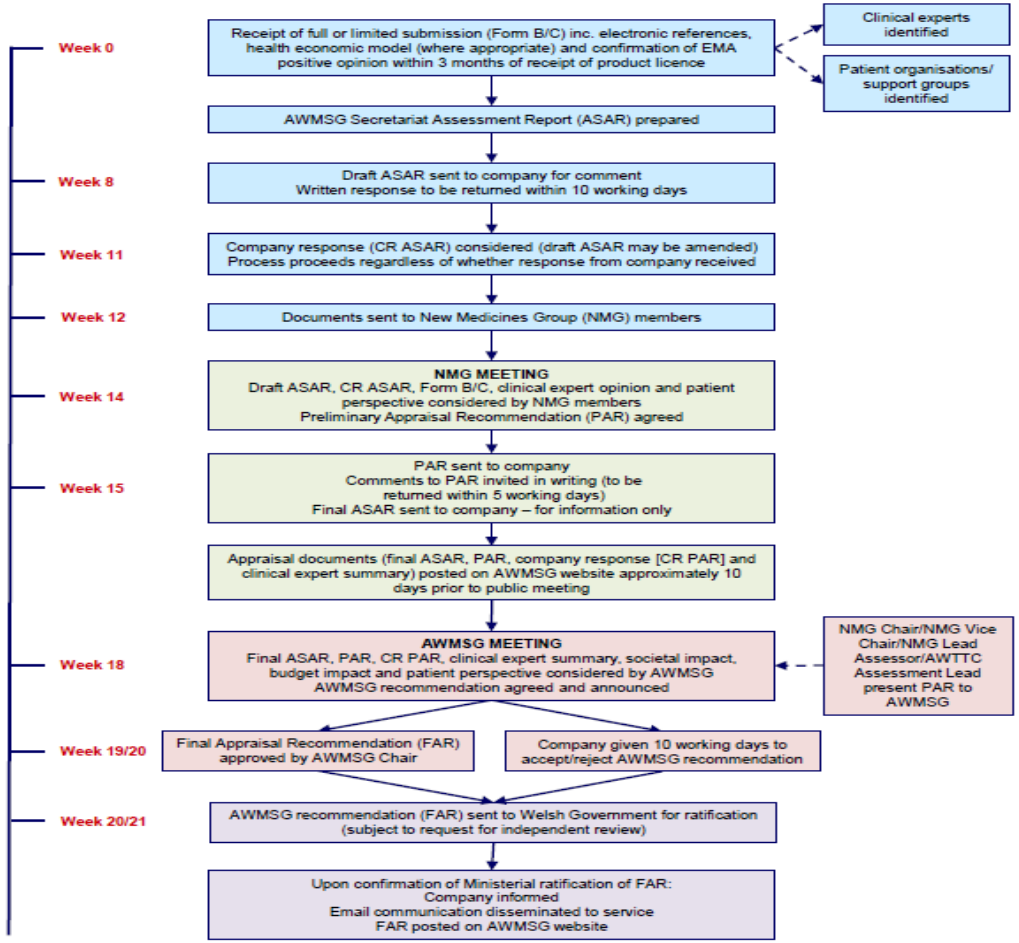
The Company Submission – AWTTC's role

Tony Williams

All Wales Therapeutics and Toxicology Centre

AWTTC
All Wales Therapeutics & Toxicology Centre




Week 0
Receipt of full or limited submission (Form B/C) inc. electronic references, health economic model (where appropriate) and confirmation of EMA positive opinion within 3 months of receipt of product licence
Clinical experts identified
Patient organisations/ support groups identified
AWMSG Secretariat Assessment Report (ASAR) prepared
Week 8
Draft ASAR sent to company for comment
Written response to be returned within 10 working days
Week 11
Company response (CR ASAR) considered (draft ASAR may be amended)
Process proceeds regardless of whether response from company received
Week 12
Documents sent to New Medicines Group (NMG) members
Week 14
NMG MEETING
Draft ASAR, CR ASAR, Form B/C, clinical expert opinion and patient perspective considered by NMG members
Preliminary Appraisal Recommendation (PAR) agreed
Week 15
PAR sent to company
Comments to PAR invited in writing (to be returned within 5 working days)
Final ASAR sent to company – for information only
Appraisal documents (final ASAR, PAR, company response [CR PAR] and clinical expert summary) posted on AWMSG website approximately 10 days prior to public meeting
Week 18
AWMSG MEETING
Final ASAR, PAR, CR PAR, clinical expert summary, societal impact, budget impact and patient perspective considered by AWMSG
AWMSG recommendation agreed and announced
NMG Chair/NMG Vice Chair/NMG Lead Assessor/AWTTC Assessment Lead present PAR to AWMSG
Week 19/20
Final Appraisal Recommendation (FAR) approved by AWMSG Chair
Company given 10 working days to accept/reject AWMSG recommendation
Week 20/21
AWMSG recommendation (FAR) sent to Welsh Government for ratification (subject to request for independent review)
Upon confirmation of Ministerial ratification of FAR:
Company informed
Email communication disseminated to service
FAR posted on AWMSG website

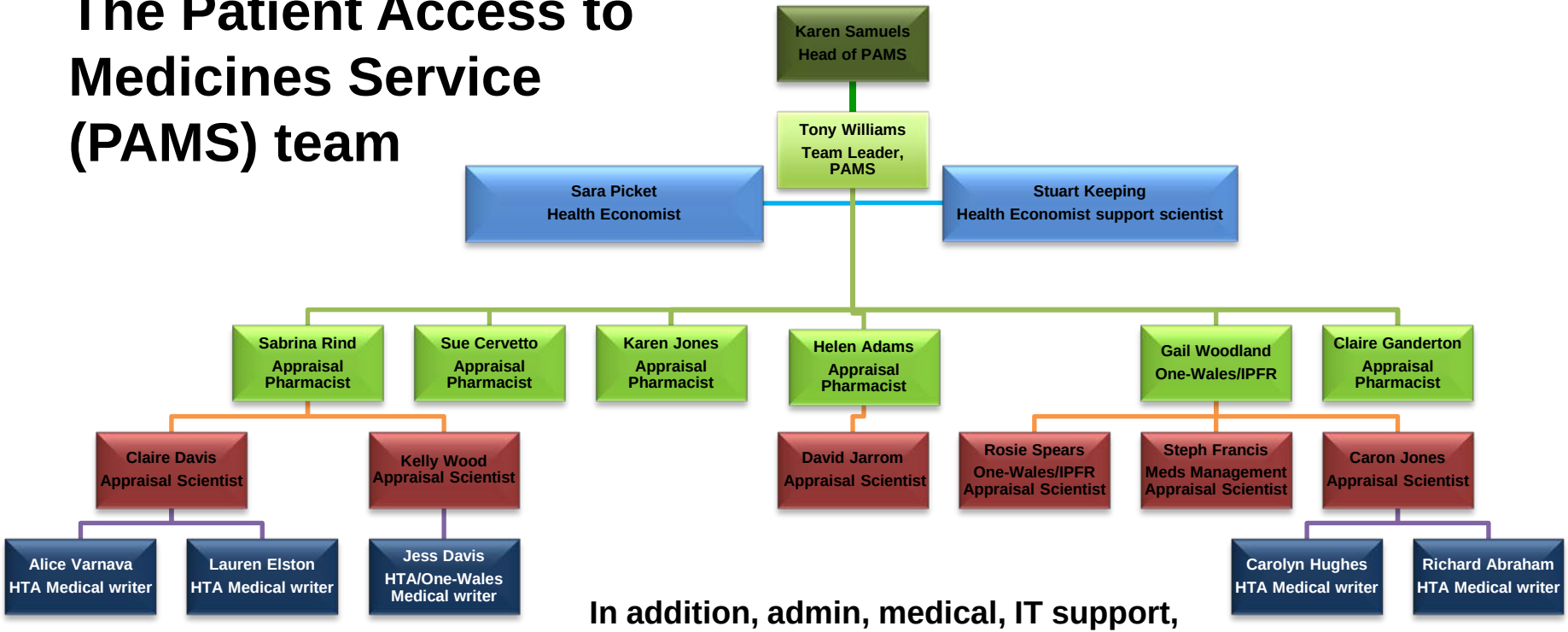
Overview

- AWTTC staff
- Data capture and engagement pre-submission
- Initial assessment of the company submission
- Writing of the assessment report
- Role of AWTTC at committee meetings
- Reviewing of AWMSG advice

AWTTC ‘Front of House’

- All queries are routed via email through the AWTTC generic account: AWTTC@Wales.NHS.UK or dealt with directly by Ruth - liaison manager
- Queries requiring input from the professional team are routed to Duty Managers (appraisal pharmacist and appraisal scientist on a rota basis) supported by the senior management team as required
- Majority of enquires are replied to on the same day

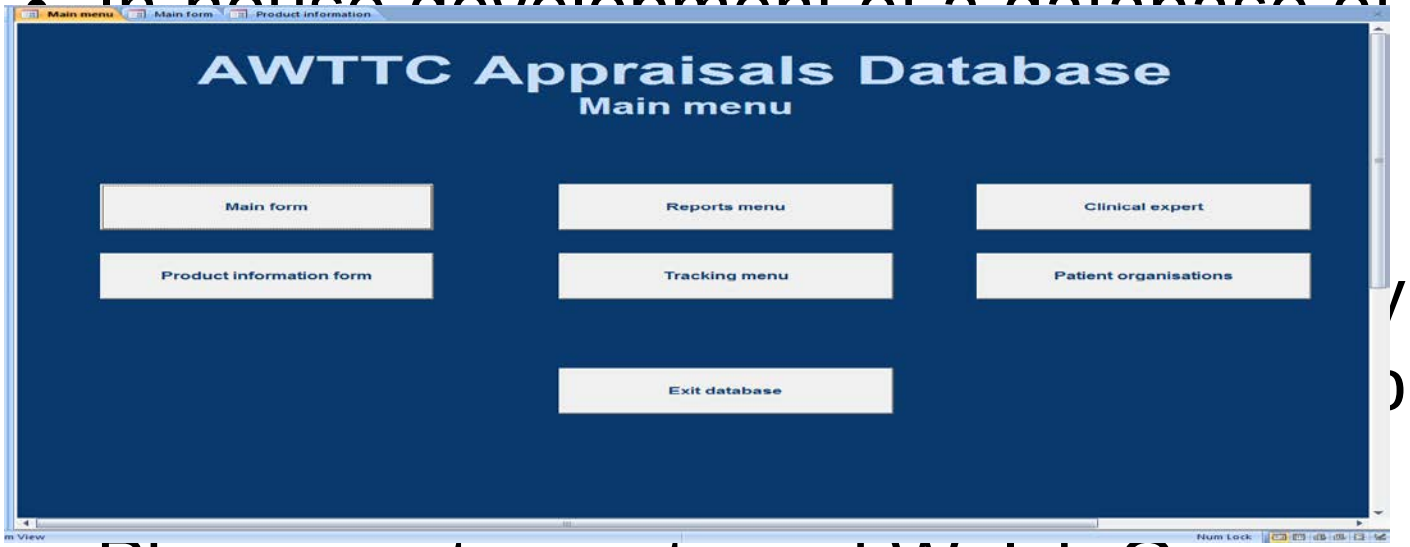
The Patient Access to Medicines Service (PAMS) team



In addition, admin, medical, IT support, and financial forecasting/WPAS/horizon scanning support from WAPSU

Data capture

- In house development of a database of



rts for

Pharmacist reports and Welsh Government e.g. CMO update, WG monthly reports

Search by: Ref No | Generic name | Trade name

Product information

Add new product | Delete this product | Today's tracking | NSDF | Main form | Close form

Generic name	cabozantinib	Trade name	(Cometriq®)	Ref No	577
Directory	S:\Welsh Medicines Partnershi				
Status	05a	Keyword	thyroid		

Indication: Treatment of adult patients with progressive, unresectable locally advanced or metastatic medullary thyroid carcinoma. For patients in whom Rearranged during Transfection (RET) mutation status is not known or is negative, a possible lower benefit should be taken into account before individual treatment decision

Previous entry | Associated diseases | Next entry

General information | Company contact details | NICE | SMC | Horizon scanning

Abbreviated indication: Treatment of adult patients with progressive, unresectable locally advanced or metastatic medullary thyroid carcinoma. For patients in whom Rearranged during Transfection (RET) mutation status is not known or is negative, a possible lower benefit should be taken into account before individual treatment decision

Record added by	Stephanie	Date added	22/06/2009
Formulation	capsule		
Identified by	Horizon Scanning	Technology type	New product
BNF category	Malignant disease and immunosupression		
CHMP date	19/12/2013	EMA date	21/03/2014
UK licence date	21/03/2014	Licence withdrawn date	
UK launch date			

Product strength and formulations

BNF subsection: 8.1.5

Cancer medicine?: Cancer

EMA orphan status ☑ | Cancer drugs fund ☑ | Website enabled ☑

Appraisal status: Company intend on submitting 18th July 2014

Status after consideration:

Main menu | Main form | NSDF Tab Style V2 | Product information | Associated diseases

Search by: Ref No | Generic name | Trade name

Product information

Add new product | Delete this product | Today's tracking | NSDF | Main form | Close form

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Previous entry | Associated diseases | Next entry

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NICE status	In progress	NICE advice code		NICE advice date		Date checked	29/11/2016
Appraisal type	Multiple Technology Appra	NICE appraisal ID	ID56	Advice due	Jan 2018	Did NICE consider a PAS?	
NICE advice reviewed		Review outcome		NICE review code		Review date	

NICE link: https://www.nice.org.uk/guidance/indevelopment/gid-ta10082

NICE information: Cabozantinib and vandetanib for treating unresectable locally advanced or metastatic medullary thyroid cancer [ID56]

NICE versus AWMSG advice

Record: 538 of 3100 | No Filter | Search

Main menu | Main form | NSDF Tab Style V2

Search by: Ref No | Generic name: cabozantinib | Trade name

Main form

Today's tracking | NSDF | Product info | Close form

Generic name: cabozantinib | Trade name: (Cometriq®) | Ref No: 577 | Directory: S:\Welsh Medicines Partnership

Status: 05a | Keyword: thyroid

Indication: Treatment of adult patients with progressive, unresectable locally advanced or metastatic medullary thyroid carcinoma. For patients in whom Rearranged during Transfection (RET) mutation status is not known or is negative, a possible lower benefit should be taken into account before individual treatment decision

Previous entry | Next entry

Search | Summary | Company contact | Form A details | PAS information | Appraisal information | NMG outcomes | AWMSG Advice

Form A requested: 10/01/2014 | Initial Form A date: 13/06/2014 | Final Form A date: 13/06/2014 | Appraisal monitoring

Abbreviated indication: Treatment of adult patients with progressive, unresectable locally advanced or metastatic medullary thyroid carcinoma. For patients in whom Rearranged during Transfection (RET) mutation status is not known or is negative, a possible lower benefit should be taken into account before individual treatment decision

CHMP date: 19/12/2013 | EMA date: 21/03/2014 | UK licence date: 21/03/2014 | Licence withdrawn date: | UK launch date:

Formulation: capsule | Product strengths

NICE status: In progress | PAS in submission: ☐

Cost information: xxxx per patient per year (ex VAT) based on £xxxx (ex VAT) per month irrespective of patient weight. There are no additional costs expected with the use of the new medicine/year.

Comparators suggested by company: CAPRELSA (Vandetanib)

EMA orphan status: ☑

Comparator search status: Completed

Company considers medicine meets ultra orphan/rare disease:

Company estimate of patient

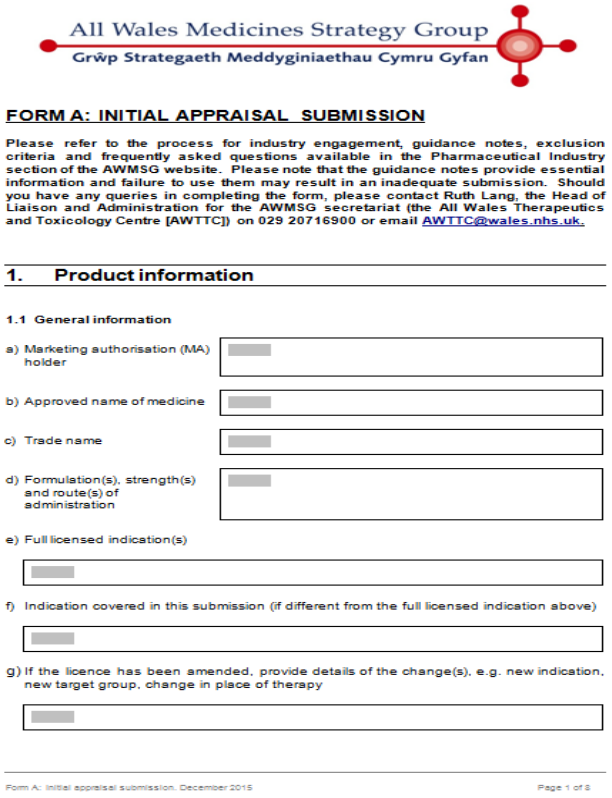
Company considers medicine

Comparators

Record: 538 of 3100 | No Filter | Search

Pre-submission

- Although the onus is on the company to engage in the AWMSG process, AWTTC staff actively monitor for medicines approaching marketing authorisation
- Companies are contacted to submit an initial submission form (Form A) around the time of CHMP positive opinion
- Support is offered for those companies who indicate difficulties with progressing a submission



All Wales Medicines Strategy Group
Grŵp Strategaeth Meddyginiaethau Cymru Gyfan

FORM A: INITIAL APPRAISAL SUBMISSION

Please refer to the process for industry engagement, guidance notes, exclusion criteria and frequently asked questions available in the Pharmaceutical Industry section of the AWMSG website. Please note that the guidance notes provide essential information and failure to use them may result in an inadequate submission. Should you have any queries in completing the form, please contact Ruth Lang, the Head of Liaison and Administration for the AWMSG secretariat (the All Wales Therapeutics and Toxicology Centre [AWTTC]) on 029 20716900 or email AWTTC@wales.nhs.uk.

1. Product information

1.1 General information

a) Marketing authorisation (MA) holder

b) Approved name of medicine

c) Trade name

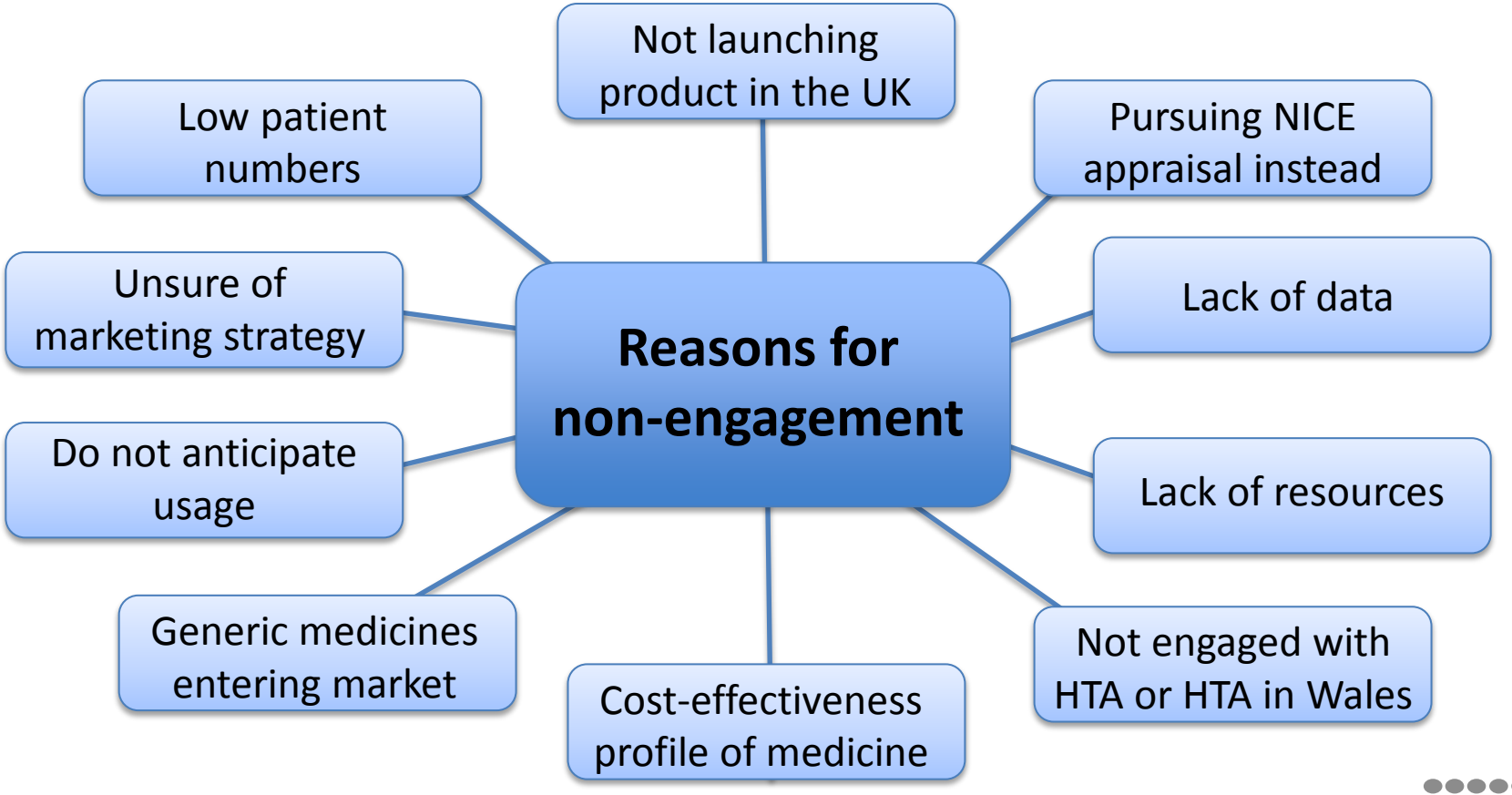
d) Formulation(s), strength(s) and route(s) of administration

e) Full licensed indication(s)

f) Indication covered in this submission (if different from the full licensed indication above)

g) If the licence has been amended, provide details of the change(s), e.g. new indication, new target group, change in place of therapy

Form A: Initial appraisal submission, December 2015 Page 1 of 8


Reasons for non-engagement
Not launching product in the UK
Low patient numbers
Pursuing NICE appraisal instead
Unsure of marketing strategy
Lack of data
Do not anticipate usage
Lack of resources
Generic medicines entering market
Not engaged with HTA or HTA in Wales
Cost-effectiveness profile of medicine

‘Form A’ stage: NSDF

- NSDF = New Submission Decision Form
- Decision process for deciding whether a medicine meets criteria for appraising and if so, whether it should be a full or limited submission
- Aim is to provide a decision within two of Form A
- Each submission is checked against the latest exclusion criteria, decision process for a full or limited submissior and projected costs are verified

Main menu | Main form | NSDF Tab Style V2

Search by: Ref No | Generic name | Trade name

NSDF | Product information for this product | Main form for this product | Comparators | Close form

Generic name	cabozantinib	**Trade name**	(Cometriq®)	**Ref No**	577	**Directory**	S:\Welsh Medicines Partnershi
Status	05a			**Keyword**	thyroid		

Indication Treatment of adult patients with progressive, unresectable locally advanced or metastatic medullary thyroid carcinoma. For patients in whom Rearranged during Transfection (RET) mutation status is not known or is negative, a possible lower benefit should be taken into account before individual treatment decision

General information | Processing | Decision comments | NSDF decision | NSDF action

NSDF comments

PAS included in submission ☐

The company are not considering a PAS. The company views this medicine as first line treatment. The estimated number of patients per year based on Cancer Research UK thyroid cancer incidence in Wales of which is estimated that 2% of these thyroid cancers are diagnosed as metastatic medullary thyroid carcinoma. The company views the medicine having ultra-orphan status and EoL policy. Please read rationale from Form A (pg 4). The company have pointed out that carbozantinib is indicated for short life expectancy, whereby patients in the placebo group had a median duration of overall survival (OS) of 20.3 months (based on an administrative analysis of OS was conducted with data up to June 15th, 2012, based on 162 (75%) of the 217 deaths required for the final analysis), less than the 24 months median survival set out in the AWMSG/NMG criteria There is sufficient evidence to indicate that the COMETRIQ offers an extension to life of at least

Pharmacist decision on submission required

Date of pharmacist comments

New medicine. Form B. Please also check strength of product…20 and 80mg on database, 20mg on SPC sent is there an SPC for 80?

Medical director decision on submission required

Date of med director comments

New chemical entity Form B. Comparator Caprelsa (due for appraisal AWMSG 3.9.14). End of life applies XL184-301 trial company states 5.7/12 increase OS and placebo goup 20.3/12.
Ultraorphan does not apply according to current AWMSG guidelines. Orphan indication approved by EMA 21.03.14 incidence stated 0.7/10,000 i.e 3.5/50,000. Available in England ask SAG for opinon on comparators and opinion on clinical need.
RB 4.8.14 Comparator Best supportive care and Vandetanib

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‘Form A’ stage: NSDF

Areas of difficulty can include:

- Does it meet exclusion criteria? e.g. antidote, biosimilar, very minor licence extension, overlap with current or upcoming NICE guidance
- Acceptance of a limited submission: companies will often argue the case for a pragmatic approach to be taken
- Is there a PAS/WPAS associated with the medicine?
- Is budget impact considered significant?
- The comparator appropriate?
- Consistency with previous decisions

The Form B/C submission

- If the AWMSG exclusion criteria are not met, AWTTC request Form B/C from the company

- Upon receipt, the company submission is reviewed by the AWTTC medical advisor, appraisal pharmacist and a health economist at Bangor University

Is the submission appropriate for the licensed indication?

Have the correct comparators been used?

Has the company restricted their submission?

Is the health economic model present and complete?

Does the End of Life criteria apply?

Is the health economic measure/model appropriate?

Does the orphan/ultra-orphan policy apply?

Is the population data appropriate for Wales?

Is the information on budgetary impact satisfactory?

The Form B/C submission

- AWTTC highlight any areas where the company may strengthen their submission; examples include:
  - Choice of comparator
  - Increased evidence to be able to appraise the full indication
  - The need for a full rather than limited submission
  - Choice of health economic model; CUA versus CMA
  - Evidence surrounding EoL or orphan/ultra-orphan status

- The company are informed that AWTTC can only advise on their approach and it is the decision of the committees to decide on whether their approach is justified

- Evidence fro is summarised and critiqued to p ariat Assessment Report (ASAR sidered include the company refe and results of an independent li
- The clinical se over a 5 day period and is subsequ itor (Pharmacist) and a technica
- A pool of health o write the health economic sectio r reviewed by the health economic
- Proofed by men management team

AWTTC at NMG

- Assessment lead provides notes containing key points for NMG chair
- Assessment lead presents any issues raised by applicant company and clinical experts and responds to any queries regarding process/clarify evidence
- Points raised by NMG members are documented and form part of AWMSG briefing notes for the AWMSG Chair and Head of HTA
- ASAR may be updated in line with comments or corrections provided by committee members
- Draft PAR for Form C agreed prior to NMG

AWTTC at AWMSG

- Assessment lead highlights key points and presents any issues raised by applicant company and clinical experts
- Responds to any queries regarding process/ clarification of the evidence
- Ensure that there is consistency with wording and process
- Liaises with the company representatives before, during and subsequent to the meeting

Main menu | Main form | NSDF Tab Style V2

Search by:

Ref No | Generic name: cabozantinib | Trade name

Main form

Today's tracking | NSDF | Product info | Close form

Generic name: cabozantinib | Trade name: (Cometriq®) | Ref No: 577 | Directory: S:\Welsh Medicines Partnership

Status: 05a | Keyword: thyroid

Indication: Treatment of adult patients with progressive, unresectable locally advanced or metastatic medullary thyroid carcinoma. For patients in whom Rearranged during Transfection (RET) mutation status is not known or is negative, a possible lower benefit should be taken into account before individual treatment decision

Previous entry | Next entry

Search | Summary | Company contact | Form A details | PAS information | Appraisal information | NMG outcomes | AWMSG Advice

AWMSG advice

Cabozantinib (Cometriq®) is recommended as an option for use within NHS Wales for the treatment of adult patients with progressive, unresectable locally advanced or metastatic medullary thyroid carcinoma. For patients in whom Rearranged during Transfection (RET) mutation status is not known or is negative, a possible lower benefit should be taken into account before individual treatment decision.

Option for use ☑ | Company informed ☐ | Website-enabled ☑ | Enable for website

Status after consideration:

Review process initiated ☐ | Review information | Review reports menu

Statement of Advice posted ☑ | Statement of advice information

Website link:

EMA orphan status ☑ | AWMSG considered end of life criteria ☐ | AWMSG considered ultra orphan/rare disease: Ultra orphan

Advice no	4014
Posted to website date	29/01/2015
Ministerial ratification date	28/01/2015
Service notified date	29/01/2015
Statement of advice date	13/08/2014
DAS date	
Date of next review	28/01/2018
Date of last review	

Record: 538 of 3100 | No Filter | Search

Updating AWMSG advice

- Following recommendations from NICE accreditation a review process has now been developed and a review team has been set up within AWTTC
- All advice is reviewed after three years of initial advice being issued.
- Literature search conducted and close liaison with the applicant company and clinical experts takes place
- Consideration is given whether it is appropriate to amalgamate advice

Updating AWMSG advice

Recommendation of AWMSG

Insulin detemir (Levemir®) is recommended as an option for use within NHS Wales for the treatment of diabetes mellitus in children aged 2–5 years.

- Licence extended to include 1-2 year olds
- Advice reviewed and updated

Recommendation of AWMSG

Insulin detemir (Levemir®) is recommended as an option for use within NHS Wales for the treatment of diabetes mellitus in children aged 1–5 years.

- Changing landscape within NICE
- New Treatment Fund and closer engagement with Pharma and NHS Wales for horizon scanning and financial forecasting
- Earlier engagement with companies with further refinement of the appraisal process to ensure advice is timely
- Strengthen links between HTA and One-Wales processes

Thank you

AWTTC
All Wales Therapeutics & Toxicology Centre