Crystallise Insights

HTANGEL:
AN OVERVIEW OF RECENT HTA DECISIONS

"A key element in generating a successful submission for a new asset is understanding how HTA bodies have responded to similar technologies, so pitfalls can be avoided and winning strategies adopted."

Alison Martin, Director

Key messages

HTAngel summarises new HTA decisions each month

Since May 2023, Crystallise has been producing a monthly summary of decisions made by 32 Health Technology Assessment (HTA) bodies around the world (see Table 2. List of HTA organisations by country.). The newsletter, HTAngel, is published on the Crystallise website, and you can subscribe to the monthly newsletter here.

The race for HTA approval is highly competitive.

Between May 2023 and January 2024, there were at least **two** separate HTA decisions for **eight** different therapies for lymphoma, **five** for non-small-cell lung cancer, **four** for multiple myeloma, **three** for prostate cancer, **three** for breast cancer and **three** for haemophilia. This is in addition to any older treatments that had already been approved for these indications.

Some HTA bodies are harder to win over than others.

For those pharmaceutical therapies that were accepted by some but not all HTA bodies, *Haute Autorité de Santé* (HAS) in France approved 70%, *National Institute for Health and Care Excellence* (NICE) in England and the *Scottish Medicines Consortium* (SMC) each approved 68%, while the *Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen* (IQWiG) in Germany and the National Commission for the Incorporation of Technologies in the Unified Health System (CONITEC) in Brazil only approved 29% each.

There are grounds for optimism.

Despite the crowded market, the majority of new pharmaceutical technologies were approved for use in at least one country, and only 11% were rejected by all HTA bodies who evaluated them. Even where a technology was initially rejected, a later submission was successful in some cases, possibly following an arrangement that reduced costs or risk for the purchasers.

Although HTA bodies vary in their willingness to approve a new asset, some products are always going to struggle for market access.

New technologies for genetic or metabolic diseases and cancers were the most likely to be approved. However, within the same disease area, some assets were more successful than others. For example, of the eight drugs that were assessed for lymphoma in more than one country during our analysis period, two were approved by all HTA bodies that reviewed them.

The challenges of successful market access

Health Technology Assessment (HTA) bodies have a big impact in determining whether a newly-launched technology is profitable. By determining whether the new technology is good value for healthcare payers' money, they provide guidance for clinicians on whether they should prescribe the new drug or refer patients for a new diagnostic test or procedure.

"With average costs of developing a new drug up to $4.54 billion in 2019 US dollars[1], it is obvious why getting HTA approval for a new treatment can make the difference between financial success and failure."

Manufacturers invest considerable money and resources into collating and presenting the evidence to support their submissions for HTA approval, and a whole industry of Health Economics and Outcomes Research is based on catering to that demand. A key element in generating a successful submission is understanding how HTA bodies have responded to similar technologies, so pitfalls can be avoided and winning strategies adopted.

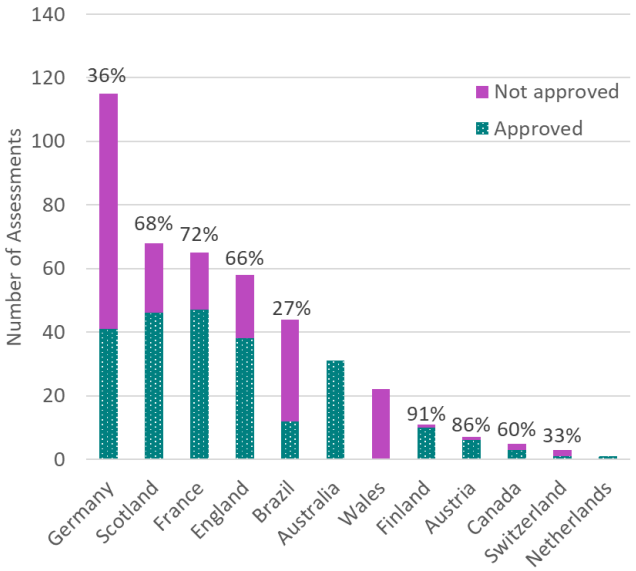
Some HTA bodies are more prolific and accepting than others

In the first nine months during which we collected data, there were 550 reports published by the 32 HTA bodies we have surveyed, of which 77% were for pharmaceutical and biological technologies, 13% non-pharmacological technologies, and 8% diagnostic technologies.

IQWiG in Germany was the most prolific body, with 115 HTA decisions on pharmaceutical products in the 9 months, followed by the SMC in Scotland (68), HAS in France (65) and NICE in England (58).

Percentages refer to approval rate over this period

For the rest of this report, we will focus on HTA decisions related to pharmaceutical technologies, including biological and gene therapies.



Approval rates generally ranged from 27% (in Brazil) to 91% (in Finland). However, some bodies, such as the *Australian Government Department of Health and Aged Care*, only publish approvals, and we can't determine from the website how many assessments ended up being rejected. Similarly, only one assessment has been identified for *Zorginstituut Nederland* so far, so no conclusions can be drawn from its 100% acceptance rate. The *All Wales Medicines Strategy Group* (AWMSG) typically defers to NICE in England for most decisions, with submissions generally excluded from assessment (and technically therefore not approved by AWMSG).

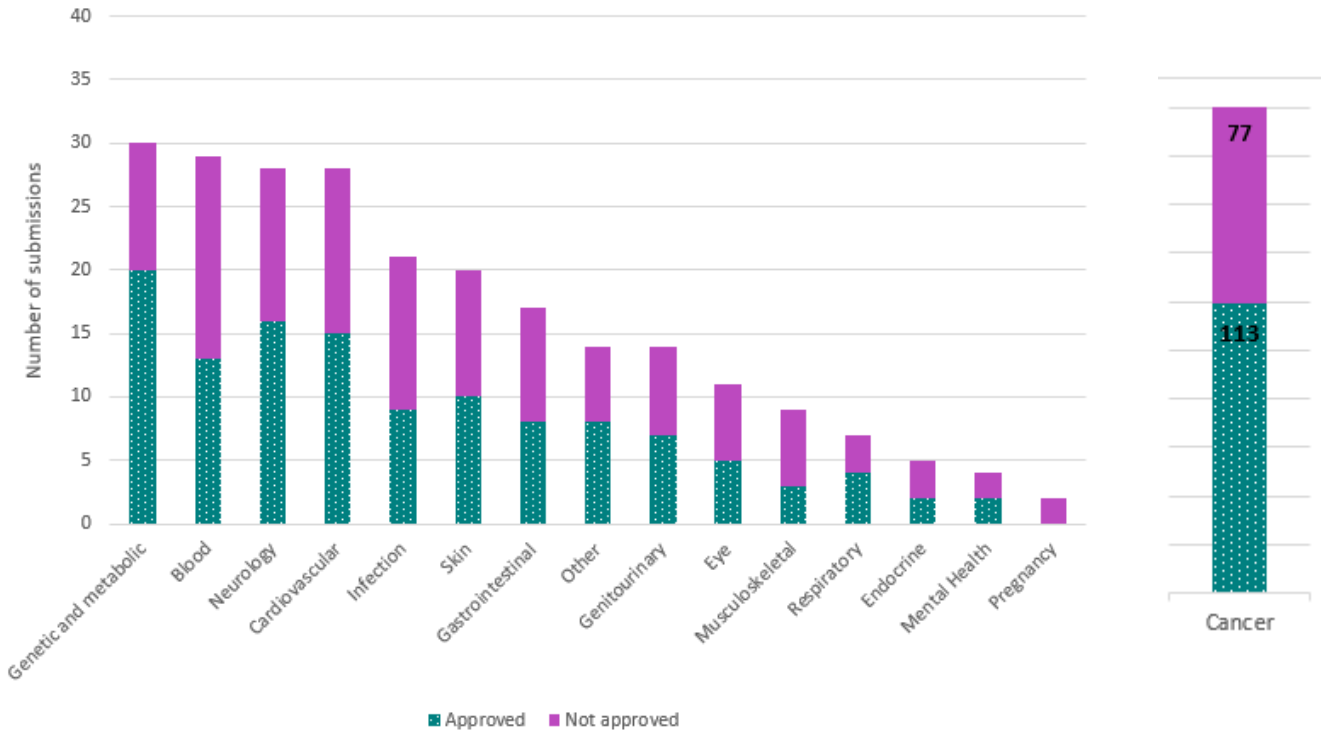
HTA bodies are focused on cost-effectiveness rather than efficacy

"Drugs that significantly enhance quality of life or extend life beyond current treatments stand the best chance of proving to be cost-effective."

HTA bodies consider a drug's cost-effectiveness beyond just efficacy and safety. Cost-effectiveness is determined based on whether the increase in cost of the new drug is balanced by an equally large increase in quality and duration of life. A new drug for a disease with no existing effective therapy, which can usually show a large improvement in quality of life, is more likely receive approval compared to a drug entering a market with numerous effective and well-tolerated treatments, particularly when several of these alternatives are off-patent and available as inexpensive generics.

New therapies for genetic/metabolic diseases and cancers were most likely to be approved

New drugs for diseases that have a big impact on patients' quality of life and those that prolong life more than existing treatments are therefore most likely to be shown to be cost-effective and are therefore most likely to be prioritised for development by manufacturers. Not surprisingly, therefore, there were far more submissions for cancer therapies than for any other disease type, with the next most common areas of genetic and metabolic disorders, blood disorders, neurological disorders and cardiovascular diseases trailing a long way behind.



Approval rates were 59% for cancer treatments. Across the other indications, approval rates were highest for genetic and metabolic disorders (67%), perhaps reflecting that these are generally rare diseases with few existing approved treatments. Of the other disease areas, only cancer (59%), neurology (57%), respiratory (57%) and cardiovascular diseases (54%) had more than 50% approval. Musculoskeletal disorders (33%) and pregnancy (0% of just 2 submissions) had the lowest approval rates.

HTA bodies tend not to agree with each other

Manufacturers will generally want to seek HTA approval in more than one region. The order in which submissions are made may depend on company-specific local factors, such as whether they will hold the authority to market the drug in that country directly or if another company will own those rights, and the size of their local sales force. Manufacturers may also want to start by targeting the countries where they expect to have the biggest market, either due to greater disease prevalence or to local prescribing practices making it easier for a new drug to dominate. However, they may also be swayed by the chances of success with each HTA body. Approval in one country is no guarantee of approval in others.

"Of 75 treatments that were reviewed by 2 or more HTA bodies over the 9 months, 32% were approved by all that evaluated them, 11% were rejected by all and 57% had mixed success."

Only a third of new technologies were approved by all HTA bodies that evaluated them

Seventy-five pharmaceutical products received decisions from two or more HTA bodies for a specific disease between May 2023 and January 2024. Of these, 24 (32%) were approved by all HTA bodies, eight (11%) were rejected by all the HTA bodies or had the submission terminated by the manufacturer. The remaining 43 drugs (57%) had mixed success.

✓ *Approved;* ✗ *Not approved;* ≠ *Excluded, or submission terminated;* ± *mixed results*

Table 1. Technologies assessed.

Technology	Indication	Australia	Austria	Brazil	England	Finland	France	Germany	Netherlands	Scotland	Wales	Success score
Darolutamide	Prostate cancer	✓			✓			✓		✓		4
Trastuzumab deruxtecan	Breast cancer					✓	✓	✓		✓		4
Brexucabtagene autoleucel	ALL				✓		✓			✓		3
Durvalumab	Biliary cancer						✓	✓		✓	≠	3
Glofitamab	Lymphoma	✓					✓	✓			≠	3
Nivolumab	NSCLC					✓	✓	✗		✓		3
Pembrolizumab	Endometrial, colorectal, gastric, small intestine and biliary cancers		✓	✗	✓					✓		3
Rimegepant	Migraine	✓			✓					✓	≠	3
Risankizumab	Crohn's disease				✓			✓		✓		3
Sacituzumab bigovitecan/ govitecan	Breast cancer					✓	✓	✓				3
Selpercatinib	NSCLC	✓			✓					✓		3
Zanubrutinib	CLL				✓		✗	✓		✓	≠	3
Atogepant	Migraine	✓								✓		2
Avacopan	Vasculitis	✓								✓		2
Avalglucosidase alfa	Pompe disease						✓			✓		2
Burosumab	Hypophosphatemia						✓			✓		2

Technology	Indication	Australia	Austria	Brazil	England	Finland	France	Germany	Netherlands	Scotland	Wales	Success score
Concizumab	Haemophilia A or B	✓					✓					2
Dapagliflozin	Heart failure				✓			±		✓		2
Deucravacitinib	Psoriasis				✓			×		✓	≠	2
Dostarlimab	Endometrial cancer		✓				✓					2
Empagliflozin	Kidney failure				✓			×		✓		2
Epcoritamab	Lymphoma						✓	✓			×	2
Ivosidenib	AML	✓						✓				2
Ivosidenib	Biliary cancer						✓	✓				2
Lisocabtagene maraleucel	Lymphoma						✓	✓				2
Lumacraftor/ ivacaftor	Cystic fibrosis						✓	✓				2
Mavacamten	Cardiomyopathy				✓		✓	×			≠	2
Olaparib	Prostate cancer				✓			✓			≠	2
Olaparib	Breast cancer				✓					✓		2
Semaglutide	Obesity				✓		≠			✓		2
Setmelanotide	Bardet Biedl syndrome						✓	✓		×		2
Tebentafusp	Melanoma					✓	✓					2
Tisagenlecleucel	Lymphoma				≠		✓	✓				2
Upadacitinib	Crohn's disease				✓			×		✓	≠	2
Ustekinumab	Crohn's disease	✓		✓								2
Voclosporin	Lupus nephritis				✓			×		✓		2
Vutrisiran	Amyloidosis						✓			✓		2
Amivantamab	NSCLC						✓			×		1

Technology	Indication	Australia	Austria	Brazil	England	Finland	France	Germany	Netherlands	Scotland	Wales	Success score
Axicabtagene ciloleucel	Lymphoma				±		✓	×		×		1
Belantamab mafodotin	Myeloma							✓		×		1
Bimekizumab	Spondyloarthritis							×		✓		1
Bimekizumab	Psoriatic arthritis							×		✓		1
Ciltacabtagene autoleucel	Myeloma				≠			✓				1
Cipaglucosidase alfa	Pompe disease							×		✓		1
Cipaglucosidase alfa and miglustat	Pompe disease				✓		×					1
Daratumumab + bortezomib	Myeloma			×	✓							1
Dupilumab	Prurigo						✓	×				1
Dupilumab	Atopic dermatitis						✓	×				1
Durvalumab	Hepatocellular carcinoma		✓					×				1
Efgartigimod alfa	Myasthenia gravis						✓			×		1
Emicizumab	Haemophilia A			±			✓	×				1
Esketamine	Depression				≠			✓				1
Etranacogen dezaparvovec	Haemophilia B						×	✓				1
Ibrutinib	CLL							×		✓		1
Lasmiditan	Migraine							×	✓			1
Lutetium-177 vipivotide tetraxetan	Prostate cancer				×			✓				1
Mirikizumab	Ulcerative colitis	✓						×			≠	1
Nivolumab	Melanoma						×	✓				1

Technology	Indication	Australia	Austria	Brazil	England	Finland	France	Germany	Netherlands	Scotland	Wales	Success score
Olaparib	Ovarian cancer				✓			✗				1
Ravulizumab	Myasthenia gravis				≠		✓					1
Risdiplam	Spinal muscular atrophy				✓			✗				1
Secukinumab	Hidradenitis suppurativa				✓			✗			≠	1
Spesolimab	Psoriasis	✓						✗				1
Tafasitamab	Lymphoma	✓			✗					✗		1
Teclistamab	Myeloma						✓	✗				1
Trastuzumab deruxtecan	Stomach cancer					✗	✓	✗				1
Zanubrutinib	Lymphoma				✓		✗					1
Cemiplimab	Cervical cancer				≠			✗			≠	0
Dupilumab	Eosinophilic oesophagitis				≠			✗				0
Durvalumab	NSCLC			✗				✗				0
Mosunetuzumab	Lymphoma				✗					✗		0
Pegunigalsidase alfa	Fabry disease							✗		✗	≠	0
Ravulizumab	Neuromyelitis optica				≠		✗	✗			≠	0
Sotorasib	NSCLC						✗	✗				0
Tixagevimab/cilgavimab	COVID-19 prevention/ treatment				✗			✗		✗		0

✓ **Approved** ✗ Not approved ≠ **Excluded, or submission terminated** ± **mixed results**

ALL: acute lymphoblastic leukaemia; AML: acute myeloid leukaemia; CLL: chronic lymphocytic leukaemia; NSCLC: non-small-cell lung cancer

The HTA websites assessed each month are listed below.

Table 2. List of HTA organisations by country.

Country	Organisation	URL
Argentina	IECS - Instituto de Efectividad Clinica Y Sanitaria	https://www.iecs.org.ar/documentos-de-tecnologias-sanitarias/
Australia	TGA - Australian Government Department of Health and Aged Care	https://www.tga.gov.au/resources/auspmd
	PBS - Pharmaceutical Benefits Scheme	https://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/pbac-outcomes
Austria	AIHTA - Austrian Institute for Health Technology Assessment	https://aihta.at/page/horizon-scanning-in-der-onkologie-berichte/en
Belgium	KCE - Belgian Health Care Knowledge Centre	https://kce.fgov.be/
Brazil	CONITEC - National Commission for the Incorporation of Technologies in the Unified Health System	https://www.gov.br/conitec/pt-br/assuntos/reunioes-da-conitec/pautas-e-atas
Canada	CADTH – CANADIAN AGENCY FOR DRUGS AND TECHNOLOGIES IN HEALTH	https://www.cadth.ca/search?s=&f%5B0%5D=project_line%3A108244&page=0
England	NICE - National Institute for Health and Care Excellence	https://www.nice.org.uk/guidance/published?ngt=NICE%20guidelines
Finland	FinCCHTA - Finnish Coordinating Center for Health Technology Assessment, Kansallinen HTA-koordinaatioyksikkö	https://oys.fi/fincchta/katsauksia-ja-suosituksia/
France	HAS – HAUTE AUTORITÉ DE SANTÉ	https://www.has-sante.fr/jcms/p_3281266/en/avis-et-decisions-sur-les-medicaments
Germany	IQWiG - INSTITUT FÜR QUALITÄT UND WIRTSCHAFTLICHKEIT IM GESUNDHEITSWESEN	https://www.iqwig.de/projekte/projekte-und-ergebnisse/#searchQuery=query=*&page=1&rows=10&sortBy=score&sortOrder=desc&facet.filter.language=de&facet.filter.search_status=de-DE_project:Bearbeitung%20abgeschlossen
International	INAHTA - International HTA database	https://database.inahta.org/
Ireland	HIQA - Health Information and Quality Authority	https://www.hiqa.ie/reports-and-publications/health-technology-assessments
Italy	AGENAS - Agenzia Nazionale per i Servizi Sanitari Regionali	https://www.agenas.it/aree-tematiche/hta-health-technology-assessment/attivita-hta/report-hta
Italy	Argomenti - Health Technology Assessment e Horizon Scanning	https://www.salute.gov.it/portale/dispositiviMedici/dettaglioContenutiDispositiviMedici.jsp?lingua=italiano&menu=tecnologie&area=dispositivi-medici&id=5175&tipologiaInput=HTA+Report&annoInput=Seleziona+un+anno&titoloInput=&btnCerca=
Korea	NECA - Center for New Health Technology Assessment	https://nhta.neca.re.kr/nhta/eng/nhtaENG0601L.ecg
Netherlands	Zorginstituut Nederland	https://english.zorginstituutnederland.nl/publications

Country	Organisation	URL
Norway	NIPH - Norwegian Institute of Public Health	https://www.fhi.no/en/overview/news/?type=con-32/cat-780,#main
Scotland	SMC - Scottish Medicines consortium	https://www.scottishmedicines.org.uk/medicines-advice/
Singapore	ACE - Agency for Care Effectiveness	https://www.ace-hta.gov.sg/resources/scientific-publications
Spain	AETS - Agencia de Evaluación de Tecnologías Sanitarias	https://publicaciones.isciii.es/unit.jsp?unitId=aets
	isciii - Instituto de Salud Carlos III	https://publicaciones.isciii.es/unit.jsp?unitId=aets
	AETSA - Evaluacion de Tecnologias Sanitarias de Andalucia	https://www.aetsa.org/produccion-cientifica/
	AQuAS - Agència de Qualitat i Avaluació Sanitàries de Catalunya	https://aquas.gencat.cat/ca/publicacions/
	ACIS - Axencia Galega de Coñecemento en Saúde	https://acis.sergas.es/cartafol/Reports
	IACS - Instituto Aragonés de Ciencias de la Salud	https://www.iacs.es/innovacion/decisiones-basadas-en-la-evidencia/publicaciones-del-area-dbe/#informes
	OSTEBA - Basque Office for Health Technology Assessment	https://www.euskadi.eus/web01-a3ikeost/en/contenidos/informacion/osteba_publicacion/en_def/index.shtml
Sweden	SBU – Swedish Agency for Health Technology Assessment and Assessment of Social Services	https://www.sbu.se/en/search/?q=&p=1&s=0&c=178
Switzerland	FOPH - Federal Office of Public health	https://www.bag.admin.ch/bag/de/home/versicherungen/krankenversicherung/krankenversicherung-leistungen-tarife/hta/hta-projekte.html
Tunisia	INEAS – THE NATIONAL AUTHORITY FOR ASSESSMENT AND ACCREDITATION IN HEALTHCARE	https://www.ineas.tn/modifier-page-publications-ets
USA	AHRQ - Agency for Healthcare Research and Quality	https://effectivehealthcare.ahrq.gov/products/search?f%5b0%5d=field_product_type_ref.tid:54
Wales	AWMSG - All Wales Medicines Strategy Group	https://awttc.nhs.wales/accessing-medicines/medicine-recommendations/

Crystallise's insights & expertise

At Crystallise, we focus on synthesising and presenting evidence in a way that provides strategic support and medical insight for our clients. Our Evidence Mapper platform is ideal for collating a wide body of evidence so clients can drill down to find the studies they need for each location and topic. If you would like to hear more about this or our many other areas of research, please feel free to reach out.

References:

1. Schlander, M., Hernandez-Villafuerte, K., Cheng, CY. *et al.* How Much Does It Cost to Research and Develop a New Drug? A Systematic Review and Assessment. *PharmacoEconomics* **39**, 1243–1269 (2021). https://doi.org/10.1007/s40273-021-01065-y

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