Supplemental Table 1. Overview of 55 initial marketing authorizations available on April 1, 2018 - EMA clinical data website for timeline assessment by WHO ATC category (as categorized by the EMA on their ECDW).

INN (Active Substance Name)	Indication WHO ATC code	Type of initial marketing authorization	Timeline modelling possible[1]	CDP timeframe CSR or CO	Study ongoing at the time of submission[3]	Healthy volunteer studies in CDP	Pediatric patient / studies in CDP	Documents on ECDW	No. of studies in CDP	Number of phase I studies
Palonosetron	A04AA05	2 Generic CDPs	No	No CSR	N/A	N/A	N/A	2 + 2	0	0
Chenodeoxycholic acid	A05AA01	Orphan (Retrospective studies)	No	Redacted	Yes	No	Yes	14	2	0
Eluxadoline	A07	Other	Yes [b,c]	2007 - 2015	Yes	Yes	No	101	14	11
Pancreas powder (Withdrawn)	A09AA02	Other	Yes [a,b]	2005 - 2014	No	No	Yes	35	7	1
Empagliflozin + linagliptin[2]	A10BD19	Other	Yes [d]	2010 - 2016	No	Yes	No	36	13	6
Saxagliptin + dapagliflozin	A10BD21	Other	Yes	2010 - 2015	Yes	Yes	No	22	6	3
Migalastat	A16AX14	Orphan	No	No CSR	N/A	N/A	N/A	0	N/A	N/A
Enoxaparin	B01AB05	2 Generic CDPs (both with same CSR)	No	Redacted	No	Yes	No	4 + 4	1	1
Albutrepenonacog alfa	B02BD	Orphan	Yes	2010 - 2015	Yes	No	Yes	45	5	1
Eftrenonacog alfa	B02BD04	Orphan	Yes	2008 - 2014	No	No	Yes	16	4	1
Human coagulation factor X	B02BD13	Orphan	No	2010 - 2013	No	No	Yes	7	2	0
Amlopipine + valsartan	C09DB01	Generic	No	2013	No	Yes	No	11	2	2
Chlorhexidine	D08AC02	Other (Article 58)	No [a]	2002 - 2012	No	Yes	Yes	6	0 (4[4])	0
Sildenafil	G04BE03	Generic	No	2009	No	Yes	No	7	1	1
Ceftazidime + avibactam	J01DD52	Other	Yes [a]	2006 - 2015	No	Yes	No	98	26	18
Ertapenem	J01DH03	Generic	No	No CSR	N/A	N/A	N/A	2	0	0
Caspofungin acetate	J02AX04	Generic	No	No CSR	N/A	N/A	N/A	2	0	0
Elbasvir + grazoprevir	J05A	Other	Yes [b,c]	2009 - 2015	Yes	Yes	No	512	73	59
Tenofovir disoproxil	J05AF07	Other	No	Redacted	No	Yes	No	4	1	1

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Emtricitabine + tenofovir disoproxil	J05AR03	2 Generic CDPs - both with same CSR	No	Redacted	No	Yes	No	4 + 4	1	1
Emtricitabine + Tenofovir Alafenamide	J05AR17	Other	Yes [c]	1993 - 2016	No	Yes	Yes	324	54	39
Emtricitabine + rilpivirine + tenofovir alafenamide	J05AR19	Other	Yes [a,b,c]	1993 - 2016	Yes	Yes	Yes	918	76	52
Sofosbuvir + velpatasvir	J05AX69	Other	Yes [b,c]	2009 - 2015	Yes	Yes	No	455	50	30
Pandemic influenza vaccine H5N1	J07BB03	Other	No	2004[5] - 2014	Yes	Yes	Yes	112	81	12
Pemetrexed	L01BA04	2 CDPs (1 Generic, 1 Other)	No	No CSR	N/A	N/A	N/A	19	0	0
Trifluridine + tipiracil	L01BC	Other	Yes [b,c]	1998 - 2015	Yes	No	No	66	15	12
Docetaxel (withdrawn)	L01CD02	Generic	No	No CSR	N/A	N/A	N/A	2	0	0
Daratumumab	L01XC	Orphan	No[a]	2007 - 2015	Yes	No	No	28	5	2
Elotuzumab	L01XC23	Other	Yes	2006 - 2015	Yes	No	No	20	9	3
Rociletinib (withdrawn)	L01XE	Other	No[a]	2011 - 2015	Yes	Yes	No	36	7	5
Osimertinib	L01XE	Other	No	2012 - 2015	Yes	No	No	104	11	9
Lenvatinib	L01XE29	Other	Yes [c]	2005 - 2015	Yes	Yes	No	205	25	15
Bortezomib	L01XX32	2 Generic CDPs	No	No CSR	N/A	N/A	N/A	2 + 2	0	0
Carfilzomib	L01XX45	Orphan	Yes	2005- 2015	Yes	No	No	115	13	4
Autologous CD34+ enriched cell fraction that contains CD34+ cells transduced	L03	Orphan	No	2000 - 2014	Yes	No	Yes	23	5	4
Ixekizumab	L04	Other	Yes	2006 - 2016	Yes	No	No	72	13	6
Begelomab (withdrawn)	L04AA35	Orphan	No	Redacted	Yes[8]	No	No	11	2	1
Infliximab	L04AB02	Biosimilar	Yes	2012 - 2015	Yes	Yes	No	15	2	1
Daclizumab	L04AC01	Other	Yes [b,c]	2004 - 2015	Yes	Yes	No	20	11	4

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Methotrexate	L04AX03	Other	No	No CSR	N/A	N/A	N/A	2	0	0
Lesinurad	M04AB05	Other	Yes	2008 - 2014	Yes	Yes	No	246	45	30
Alendronic acid + colecalciferol (withdrawn)	M05BB03	Generic	No	Redacted	No	Yes	No	8	1	1
Drisapersen (withdrawn)	M09AX04	Orphan	No	2009 - 2014	Yes	No	Yes	105	9	1
Zonisamide	N03AX15	Generic	No	Redacted	No	Yes	No	4	1	1
Rasagiline	N04DB02	Generic	No	2009	No	Yes	No	7	1	1
Aripiprazole	N05AX12	Generic	No	2013	No	Yes	No	12	2	2
Salmeterol + fluticasone propionate	R03AK06	2 CDPs - both with same CSRs	No[a]	2008 - 2014	No	Yes	No	10 + 10	4	4
Idarucizumab	V03AB37	Other	No[a]	2012 - 2015	No	Yes	No	25	4	1
Lutetium chloride	V10X	Other	No	No CSR	N/A	N/A	N/A	2	0	0

Notes: 1.[a] Excluded from core CDP set because the CDP did not cover all 3 phases of clinical development, eg the idarucizumab CDP had no phase II CSRs. Saxagliptin + dapagliflozin scored “No” as earliest CSR documents were phase III; “No” also scored if dates redacted. CDPs were scored as “Yes” if clinical study reports had all FSI and LSO dates for all CSRs. “Yes” was also scored if interim reports for a study were available. There are additional lifecycle aspects that could not be fully integrated, eg if the corresponding EPAR indicated that: literature was used to support the market authorization (note: literature is not made available on the EMA clinical website). Additional exclusions because [b] Post-marketing, eg pharmacovigilance activities, ongoing, [c] Interventional studies planned or ongoing or, [d] studies in monotherapy CDP not included in fixed dose combination development was scored “No”.

2. Clinical study reports from 2004 available on the ECDW but the clinical development was initiated 2010 according to CO.

3. The MAH/sponsor has submitted interim reports in M.5. The EPAR or the clinical overview indicated that there were ongoing clinical studies or studies planned at the time of submission.

4. Four clinical studies - literature references – are cited in the chlorhexidine submission. As no clinical study report documents were available the score was 0.

5. Available documents for pandemic influenza vaccine H5N1 date back to 1995; however, the clinical development for the specific indication and population started in 2004.

Abbreviations: ATC=anatomical therapeutic chemical classification system, CDP=clinical development pathway; CO=clinical overview; CSR=clinical study report; ECDW= EMA clinical data website; EMA=European Medicines Agency; EPAR=European Public Assessment Report; FSI=first-subject-in; INN=international non-proprietary name, LSO=last-subject-out; N/A=not available, WHO=world health organization.