<NSAID之間的比較>

整理一下2022/10/15 right now北榮現有的NSAID

分類	ASA	Aryl acetic acids				Fenamates	Indoleacetic Acid		Aryl propionic acids		Phenyl alkanoic acids	Oxicams			COX-2 inhibitors		
															pyrazoles	bipyridines	isoxazolyl
學名	Aspirin	Aceclofenac	Diclofenac	Etodolac	Ketorolac	Etofenamate	Indomethacin	Acemetacin	Ibuprofen	Naproxen	flurbiprofen	Meloxicam	Tenoxicam	piroxicam	Celecoxib	Etoricoxib	Parecoxib
商品名	Espin EM 100 mg/cap Ropal, Aspirin "Johnson" FC 100 mg/tab	Tonec 100 mg/tab	Meitifen SR 75 mg/tab Flamquit 25 mg/tab Dicloren supp 12.5 mg	Lacoxa SR 400 mg/tab	Laston inj 30 mg/1 ml/amp Keto inj 30 mg/1 ml/amp	TEIRIA GEL 10% 40 g TEIRIA GEL 5% 40 g	Indomethacin inj 1 mg/vial (自費11000元) Indoy 25 mg/cap Indalgin 25 mg/cap	Acemet retard 90mg/cap	Ibuprofen 400mg/tab Sconin susp. MacSafe susp. (20mg/ml) 60ml/btl Pedea 10mg/2ml/amp(自費8000元)	Genuproxin 250 mg/tab	Fubifen PAP 40mg/Patch	Mobic 15mg/tab	Tencam 20mg/vial	Pirocan inj 20mg/amp Focus gel 40g	Celebrex 200g/cap	Arcoxia 60mg/tab	Dynastat inj 40 mg/vial
止痛劑量	1-4g/day 但沒人拿它止痛	100 mg BID	100-150 mg/day	400-1200 mg QD	15-30 mg Q6H <5天,兒童不宜	BID-TID	25-50mg BID-TID	90mg BID	400-800mg Q6-Q8h	250-500 mg BID	1 patch QD-TID	7.5-15mg QD	20-40 mg QD	BID-TID	200mg QD-BID	90-120 mg QD	20-40mg Q6-12H(max 80/天)
BA	50-75%(速效) @胃,小腸前段	100%	55% 有首渡代謝	≧80%	100%	外用≦20%	98%	100%	>80%	95%	很低很低 <5%	89%	100%	100%	100%	100%	100%
代謝	Esterase活化、肝conjugation	肝代謝成 diclofenac	肝3A4	Hydroxylation glucuronidate	肝氧化、conjugation		肝2C9 conjugation	肝代謝成 indomethacin	R與S態混和，肝代謝成活性S態	肝1A2, 2C8, 2C9	-	肝2C9, 3A4	肝2C9	肝2C9	肝2C9	肝3A4	肝3A4, 2C9 →valdecoxib
腎排	85%	66%	65%	73%	92%	35% (65%膽排)	60%	40%	45-79%	95%	90%	90%	65%	~90%	<3%原型	70%(<2%原型)	<5%原型
T1/2 (hr)	3hr(300-600mg) 6hr (>1g)	4 hr	2 hr	8.4 hr	5 hr(老人+30-50%) Scr 1.9-5者:11hr	14 hr	4.5 hr	1.1-4.5 hr	1.8-2 hr	12-17 hr	14-28 hr	15-20 hr	72 hr	50 hr	11 hr	22 hr	22 min
長短效	短			長	短	長	短			長							短
COX1/COX2 選擇性	非選擇,不可逆抑制 (PLT 7天)	**COX2**(97%)> COX1(46%)*	**COX-2** X0.1		**COX-1** X1-**500** (歧異高)	非選擇	**COX-1** X1~10	非選擇			**COX-1** X100	**COX-2** X0.1	**COX-1** X10	**COX-1** X10	**COX-2** X0.1	**COX-2** X0.01	**COX-2** X0.02-0.03
GI risk	++	+	+	+	++++ **X11**	?	++ ~ +++		++	+	+++(但貼片還好)	-	+	+++(外用還好)	+		=
CV risk	=	++	**+++ X1.4**	=	?	?	=		++ **X2.2**	+	=	++	=	++	**+++ X1.37**		=
健保價	2 (腸溶) 0.45 (速效)	3.3	2	9	17	52 (5%) 84 (10%)	2	2.5	2 (tab), 25 (oral susp)	2	5.3	4	30	~40(藥膏)	4.5	5.3	自費700
每日藥費	4.5~18 (速效)	6.6	2-8	9-27	17	-	4-12	5	6-16	4-8	5.3-15.9	4	30-60	?	4.5-9	5.3-10.6	700-1400
備註	• Protein binding皆>90% • 懷孕都不該用NSAID，影響宮縮與胎腎；部分可以哺乳 • aspirin不可逆抑制COX-1與COX-2，影響血小板凝集，易出血，手術前7天DC；其他NSAID多少也會影響但為可逆抑制，所以3天前DC即可。 • GI risk與CV risk每家研究做的都不一樣，僅供參考，特別mark的是我覺得比較有信心高風險者。但可以確定的是，所以有NSAID都有腎毒性、貼片局部作用較安全。																
	Onset: <1hr(速) 3-4hr (腸溶) 但腸溶並不會減少胃潰瘍風險	60%進入關節滑液 代謝成diclofenac與4'-OH-diclofenac去抑制COX	• 2顆SR就max • 預防postERCP pancreatitis可以術前給100mg supp塞劑		GI risk高，建議PRN用<5天		容易胃痛的傢伙 可用於早產兒關閉開放性動脈導管(PDA)，但可能使血液灌流減少壞死性小腸結腸炎↑有人嘗試以ibuprofen取代之		• 哺乳可 (但還是首選paracetamol) • 高劑量一樣有CV risk • 有口服劑型	• 比起ibu較少CV risk • 可以用來檢驗cancer fever			For術後痛		原型腎排%低，CCr <30可用，不太被HD洗掉 磺胺藥	CCr<30禁用	For術後痛 CCr<30盡可能低劑量使用 磺胺藥

健保給付規定 (111/7/1)

NSAIDs 精品項目 (celecoxib、nabumetone、meloxicam、etodolac、nimesulide、etoricoxib、含naproxen及esomeprazole複方製劑)

1. 使用上列尊爵不凡NSAID需符合下列條件之一：
   (1)骨關節炎病患
      Ⅰ.每日藥費<4.5元，可用於>18歲病患。
      Ⅱ.依個別成分規定如下：
         i 含celecoxib成分之Relecox 200mg僅可使用於50歲以上病患。
         ii 含nabumetone成分之No-Ton、Nabuton、Labuton及含etoricoxib之Arcoxia 60mg僅可使用於>60歲者。
         iii含etodolac成分之緩釋錠劑膠囊劑及一般錠劑膠囊劑僅可使用於60歲以上病患，惟單價低於2.25元(如Etopin、Etodon、Jenac、Doloc)且每日處方不超過2粒者，可用於18歲以上之病患。
   (2)類風濕性關節炎、僵直性脊髓炎、乾癬性關節炎等慢性病發炎性關節病變，需長期使用NSAID者。
   (3)合併有急性嚴重創傷、急性中風及急性心血管事件者。
   (4)同時併有腎上腺類固醇之患者。
   (5)曾有消化性潰瘍、上消化道出血或胃穿孔病史者。
   (6)同時併有抗擬血劑者。
   (7)肝硬化患者。
2. 使用本類製劑者不得預防性併用H2 blocker、PPI及其他消化性潰瘍用藥，亦不得合併使用前列腺素劑 (如misoprostol)。
3. nimesulide限用於急性疼痛緩解，其連續處方不得超過15日。
4. 含naproxen及esomeprazole複方製劑 不得作為急性疼痛的初始治療。

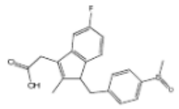
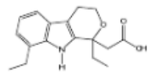
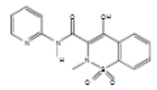
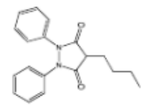
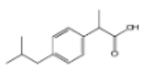
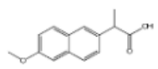
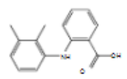
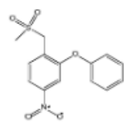
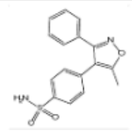
Flurbiprofen 40mg patch (如Flur Di Fen Patch)限同時符合下列條件之病患使用：
   (1)單一關節(部位)或軟組織風濕症。
   (2)不適合口服NSAID者。
   (3)不得同時併用口服或其他外用NSAID。
   (4)每月限處方16片以內。

TEIRIA * GEL 10% 40 G (Etofenamate) 健保管制藥品條件如下：
   (1)外用NSAID軟膏，不得同時併用口服或其他外用NSAID製劑，每4週至最多40G (一條)
   (2)單純局部軟組織風溼症病例不得併用口服及外用NSAID製劑

其他沒特別點名到的平凡NSAID，若沒特別說自費，則可以爽爽開健保(畢竟便宜)

破劍藥師

Table 1. Classification of NSAIDs [29].

Salicylates	Indoleacetic Acid Derivatives	Aryl Acetic Derivatives	Enolic Acids	
Acetylsalicylic acid Lysine clonixinate Benorilate Diflunisal Salicylamide Etersalate Salsalate or salicylic acid	Acemethacin Glucamethacin Indomethacin Proglumethacin Oxamethacin Sulindac Tolmetin Difenpiramide	Aceclofenac Diclofenac Etodolac Fentiazac Ketorolac Bufexamac Lonazolac Alclofenac Zomepirac	**Oxicans:** Droxicam Meloxicam Piroxicam Tenoxicam Oxaprozin Lornoxicam	**Pyrazolones:** Phenylbutazone Mofebutazone Oxyphenbutazone Kebuzone Metamizole (Dipyrone) Feprazone Nifenazone Suxibuzone Aminophenazone
				
Aspirin	Sulindac	Etodolac	Piroxicam	Phenylbutazone
Arylpropionic Derivatives		**Phenemates**	**Others**	
Butibufen Phenoprofen Phenobufen Flurbiprofen Benoxaprofen Suprofen Ibuprofen Ibuproxam	Ketoprofen Dexetoprofen Pyprophene Indoprofen Naproxen Oxaprozin Tiaprofen Dexibuprofen Phenoprofen Flunoxaprofen Alminoprofen	Meclofenamic acid Mefenamic acid Flufenamic acid Tolipanic acidNiflumic acid Etofenamate	Nabumetone Glucosamine Diacerhein Nimesulide Proquazone Azapropazone Benzidamine Orgotein Feprazone Morniflumato Tenidap Glucosaminoglycan	**Coxibs:** Celecoxib Rofecoxib Parecoxib Valdecoxib Etoricoxib 4-Aminophenol Paracetamol (Acetaminophen)
				
(S)-Ibuprofen	Naproxen	Mefenamic acid	Nimesulide	Valdecoxib

NSAID Comparison				
NSAID	**COX-2 Selectivity**	**GI Risk**	**CV Risk**	**Average Wholesale Price (AWP) / Unit ***
Salicylates				
Aspirin	Low	Moderate	Low	$0.02 - $0.10
Diflunisal	Moderate	Moderate	Unknown	$1.98 - $2.06
Salsalate	Unknown	Low	Unknown	$1.71 - $2.75
Propionic acid derivatives				
Ibuprofen	Moderate	Low	Moderate - High	$0.03 - $0.80
Ketoprofen	Low	Moderate	Unknown	$10.82
Naproxen	Low	Moderate	Low	$0.06 - $35.71
Oxaprozin	Low	High	Unknown	$3.66 - $7.73
Acetic acid derivatives				
Diclofenac	High	Moderate	High	$0.80 - $17.69
Etodolac	High	Low	Moderate	$1.29 - $3.34
Indomethacin	Low	Moderate - High	Moderate	$0.36 - $10.91
Ketorolac	Low	High	Unknown	$2.15 - $2.27
Nabumetone	Moderate	Low	Unknown	$1.23 - $58.44
Sulindac	Moderate	Moderate	Unknown	$0.94 - $1.21
Enolic acid derivatives				
Meloxicam	High	Low	Moderate	$3.10 - $31.05
Piroxicam	Moderate	High	Low	$2.60 - $4.49
Selective COX-2 inhibitor				
Celecoxib	High	Low	Moderate - High	$4.62 - $17.54

Table 2: A comparative table of cardiovascular, gastrointestinal, renal risks, pharmacokinetic, pharmacodynamics properties of non-steroidal anti-inflammatory drugs in adultsw

NSAID	CV risk	GI risk	Renal risk	COX selectivity	Absorption	Distribution	Metabolism	Elimination
ASA[1]	=	++	=	Non-selective	Rapid absorption, <1 hour Bioavailability 50-75%	Vd: 10 L Most body fluids and tissues Protein binding 90-94%	Hydrolyzed to salicylate (active) by esterases Salicylate metabolism via hepatic conjugation	Via urine Half-life 3-10 hours depending on dose
Celecoxib	++	+	=	COX2	Absorption prolonged due to low solubility Bioavailability unknown	Vd: 400 L Protein binding 97%	Hepatic via CYP2C9 and CYP3A4 CYP2C9*2 associated with reduced metabolism and elevated drug concentrations Possibly increased exposure in CYP2C9*3 carriers Inhibits CYP2D6 (40% higher metoprolol AUC increase as compared with rofecoxib)	Feces (60%) Urine (30%) Half-life 11 hours
Diclofenac	+++	++	=	Non-selective	Bioavailability 55%	Vd: 1.3-1.4L/kg Protein binding >99%	Hepatic Undergoes first-pass metabolism Forms several metabolites, one with weak activity CYP2C8 and CYP2C9 (polymorphisms not clinically significant)	Urine (65%) Bile (35%) Half-life 2 hours
Diflunisal	=	/	=	Non-selective	Well absorbed, onset ~1 hour Bioavailability unknown	Vd 7.53 L Protein binding >99%	Extensive metabolism to glucuronide conjugates	Urine (90%) Feces (<5%) Half-life 8-12 hours
Etodolac	=	+	=	Non-selective	Rapid absorption, onset ~0.5 hour Bioavailability ≥80%	Vd 0.49 L/kg Protein binding >99%	Hepatic (hydroxylation and glucuronidation)	Urine (73%) Feces (16%) Half-life 6.4 hours
Flurbiprofen	=	+++	=	Non-selective (COX1 leaning)	Rapid absorption Bioavailability 96%	Vd 0.12 L/kg Protein binding >99%	Hepatic via CYP2C9 Increased CYP2C9*3 and *5 lead to a lower clearance as compared to the wild-type *1 allele	Urine Half-life 4.7-5.7 hours
Ibuprofen	++	++	=	Non-selective	Rapid absorption, onset 0.5-1 hour Bioavailability 80%	Vd 0.12 L/kg Protein binding >99%	Hepatic via CYP2C8, CYP2C9 and oxidation Compromised clearance in carriers of two CYP2C9*3 alleles (10-30% of the enzymatic activity of the wild type) CYP2C8*3/*3 is associated with significantly decreased clearance as compared to *1/*1	Urine (45-80%) Some feces Half-life 2 hours
Indomethacin	=	+++	=	Non-selective (COX1 leaning)	Rapid and extensive absorption, onset ~30 minutes Bioavailability 100%	Vd 0.34-1.57 L/kg Crosses blood-brain barrier Protein binding 99%	Hepatic via CYP2C9 and carboxyesterase (minor pathway), but polymorphisms not clinically significant	Urine (60%) Feces (33%) Half-life 2.6-11.2 hours (7.6 hours)
Ketoprofen	=	++	=	Non-selective (COX1 leaning)	Almost complete absorption, onset <30 minutes Bioavailability ~90%	Vd 0.1 L/kg Protein binding >99%, unbound fraction doubled in hepatic impairment	Hepatic (glucuronidation) Inactive metabolite may be converted back to parent compound	Urine (80%) Half-life 2-4 hours
Meloxicam	=	+++	=	Non-selective (COX2 leaning)	Bioavailability 89%	Vd 10 L Protein binding ~99% Free fraction higher in renal failure with chronic dialysis	Hepatic via CYP2C9 and CYP3A4 (minor), forms 4 inactive meta-bolites	Urine and feces Half-life 15-22 hours
Nabumetone	=	+	=	Non-selective	Good absorption, onset after several days Bioavailability unknown	Vd 29 to 82 L Diffusion occurs readily into synovial fluid Protein binding >99%	Hepatic Prodrug metabolized into active metabolite (6MNA) Extensive first-pass effect	Urine (80%) Feces (9%) Half-life ~24 hours, increased by 50% in patients with ClCr 30-49 ml/min
Naproxen	-	++	=	Non-selective	Absorption almost 100%, onset 0.5-1 hour Bioavailability 95%	Vd 0.16 L/kg Protein binding >99%, free fraction increased in elderly	Hepatic CYP2C9 minor role in clearance although CYP2C9*3 and *5 yield a lower clearance as compared to the wild-type *1	Urine (95%) Feces (≤3%) Half-life 12-17 hours
Piroxicam	=	+++	=	Non-selective (COX1 leaning)	Well absorbed, bioavailability unknown	Vd 0.14 L/kg Protein binding 99%	Hepatic predominantly via CYP2C9, yields inactive metabolites Substrate inhibition metabolism reported predominantly for CYP2C9*1 and *3 CYP2C9*5 metabolism profile is hyperbolic	Primarily urine and feces (small amounts) Half-life 50 hours
Sulindac	=	+	=	Non-selective	Onset within a week	Crosses blood-brain barrier (brain concentrations <4% of plasma concentrations) Protein binding: 97.9% for active metabolite concentrations	Hepatic Prodrug metabolised to sulfide metabolite (active) and sulfone metabolites (inactive) Parent and inactive metabolite undergo extensive enterohepatic recirculation	Urine (50%) Feces (25%) Half-life: Sulindac 7.8 hours, Sulfide metabolite 16.4 hours
Tenoxicam	=	/	=	Non-selective (COX1 leaning)	Rapid and complete absorption, delayed with food Bioavailability 100%	Vd ~9.7 L Protein binding 98-99%	Hepatic predominantly via CYP2C9	Urine mainly Feces Half-life 72 ± 28 hours
Tiaprofenic acid	=	/	=	Non-selective	Rapid absorption, delayed with food	Protein binding ~98%	Minimal (10%) to inactive metabolites	Urine (50% unchanged drug, <10% as metabolites) Half-life ~2 hours

Color code: **Green** signifies the safer NSAID for the specific risk; **red** signifies an increased risk for the highlighted NSAID; **yellow** highlights cytochrome metabolism that is significantly affected by genetic polymorphisms

[1] At NSAID doses (not doses for secondary CV protection); - Lower risk compared to most other NSAIDs; = Risk equal/equivalent to most other NSAIDs; + Risk is slightly higher than most other NSAIDs; ++ Risk is moderately higher than most other NSAIDs; +++ Risk is substantially higher than most other NSAIDs; / Relative risk unknown or unreported in literature.