背景因子を共変量として使用することもできる。これらの共変量調整については、何らかの統計学的及び臨床的な有意性基準を用いることが望ましい。

小児での十分な予測が可能である限り、成人データを事前情報として用いた解析を考慮してもよい。

4.2.7　相互作用

従来の相互作用試験は、小児での実施を想定していない。相互作用データは、成人から外挿できる場合が多い。しかし、肝臓の発育が不完全な比較的幼い小児では、相互作用に関するデータを外挿により推定することが比較的困難な場合がある。申請者は、成人から小児の目標年齢層への相互作用データの外挿が適切であるかどうか考察すること。酵素の寄与/排泄の機序又はタンパク結合に差があると予想される場合、その影響を考察すること。このような場合、一般的な併用薬による影響及び併用薬への影響は、おそらく母集団薬物動態解析で調査することができるが、その解析には限界があることを考慮に入れること。予想外の相互作用が認められた場合、又は用量調整を推奨するためにさらなる情報が必要である場合、補助的な試験実施が必要となるかもしれない。そのような試験は、従来デザインでも、スパースサンプリングを用いたものでもよい。尿中排泄データを用いて、血中濃度データを代替又は補足できる場合がある。

4.2.8　特殊な集団：器官の機能障害及び薬理遺伝学的形質

第 4.2.7 項で述べた通り、特定経路による薬剤排泄の減少の影響は、成人と比べて幼い小児では多様であり、薬剤排泄器官の成熟度に依存すると考えられる。したがって、薬剤代謝酵素をコードする遺伝子の遺伝子多型及び肝又は腎機能障害が小児年齢層での薬物動態に及ぼす影響は、成人における影響とは異なると考えられる。

申請者は、製品特性概要（SmPC）で小児用の推奨用量を別途記載する必要性について考察しなければならない。必要性があり、可能である場合、これらの因子の影響を調査しなければならない。これは、母集団薬物動態解析を用いて実施できる。

4.3　データ解析

データ解析の主な目的は、以下の通り。

・薬物動態パラメータの推定
・様々な共変量と薬物動態パラメータとの関連性の評価
・推奨用量の探索

4.3.1　パラメータの推定

血中濃度データ（及び収集していれば尿中排泄データ）を解析し、薬剤とその活性代謝物の薬物動態を記述するパラメータを推定すること。用量調整に用いる重要な薬物動態パラメータ選択の根拠は、濃度と作用及び濃度と毒性の関係について利用可能な情報を考慮

して示すこと。パラメータは、非コンパートメント解析又はモデルによるアプローチ（非線形混合効果モデルなど）のいずれかを用いて推定できる。

4.3.2 結果の提示

データは、様々な成熟段階でのばらつきの評価を可能にし、用量調整のためのカットオフ時点の特定に役立つように提示すること。従来の非コンパートメント解析が実施されている場合、その結果を様々な年齢層での薬物動態パラメータの記述統計（平均値、SD、範囲、中央値など）、並びに様々な共変量（年齢、体重、BSA など）と個々の観察された薬物動態パラメータとの相関グラフとして提示すること。

目的とする薬物動態パラメータは、通常 AUC、C_{max}、C_{min}、CL、$t_{1/2}$、又は薬剤の有効濃度維持時間である。必要に応じて、タンパク結合の差を考慮すること。

母集団薬物動態解析を行った場合、事前に規定した解析計画、データの詳細な記述、使用した方法、モデル選択基準、及び主なモデル構築ステップの概要（経緯）を提示すること。適切なグラフによる診断（適合度、パラメータ分布など）も提示すること。その際、年齢/成熟度、体格因子などにより検討した層別評価を視覚化すること。母集団平均パラメータの推定値（標準誤差又は信頼区間）を提示すること。年齢/成熟度および体格因子などに関連した薬物動態パラメータへの影響も、視覚的に提示すること。適切なモデルのバリデーションを実施すること。

4.4 推奨投与法の開発

主要な目的は、対象患者に対して有効かつ安全と考えられる曝露量が得られることを保証する推奨用量を見い出すことである。これは、PK/PD 関係についての利用可能な情報、又は対照集団及び小児集団における曝露量と有効性/安全性とを比較したこれまでの記録に基いて検討されなければならない。どのような曝露量の変化が、用量調整の根拠となるかの目安となる規準を定めるべきであり、それは具体的な根拠に基づき、当該薬剤に特有な懸念点（有害事象又は無効）への対策を考慮したものでなければならない。小児集団における曝露量と、十分な有効性及び安全性が得られた対照群における曝露量との比較では、、曝露量範囲のすべてで有効性及び安全性の統計学的有意差を検出するのに十分な検出力がないことを考慮に入れること。

推奨用量における定常状態血漿濃度が、これまでに測定されていない場合には、投与期間中の予測曝露量のシミュレーションを行うこと。シミュレーションでは、経時的な濃度推移及び集団でのばらつきの予測に関して、図示説明を行うこと。関連する定常状態曝露パラメータの実測値又は予測値と、年齢、体重、又は他の適した共変量（ばらつきの適切な尺度など）とを比較したグラフも提示すること。新生児で見られるように、薬剤の半減期が非常に長く、即効性が求められる場合、負荷投与の可能性を検討すること。

年齢、体重、体表面積、又は腎機能等による用量調整は、臨床試験の選択基準で設定された年齢範囲より、上記の解析に基づき決定することが望ましい。用量調整に用いる共変

量の選定は、慎重に検討すること。体重別の投与を検討する場合、肥満児における過剰曝露のリスク及び患者集団における肥満児の頻度を考慮すること。用量調整の根拠となる被験者集団は、患者間のばらつきを反映するのに十分な規模でなければならない。これは、薬物動態の予測が比較的困難な年齢層（すなわち通常、年齢範囲のうち低い側）では、最も重要である。

4.5　表示

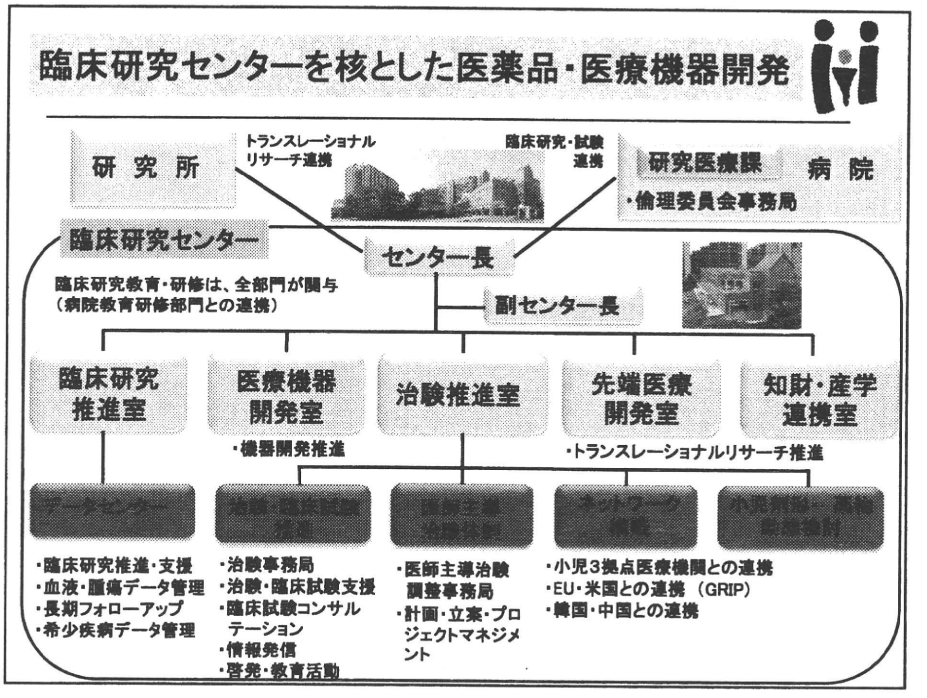
様々な年齢層の薬物動態データは、共変量が薬物動態に及ぼす影響に関して得られている情報と共に、製品特性概要（SmPC）の第 5.2 項（薬物動態）に提示すること。小児集団における推奨投与法は、SmPC の 4.2（用量）に記載すること。

小児医薬品・医療機器に関する最近の情報

国立成育医療研究センター
臨床研究センター治験推進室
中村秀文

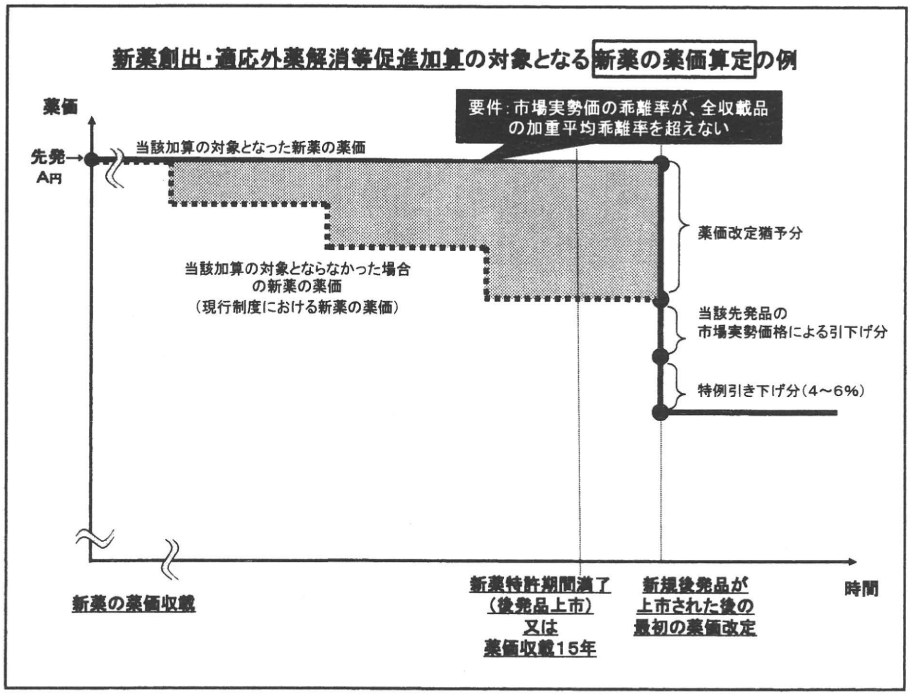
国立成育医療研究センター

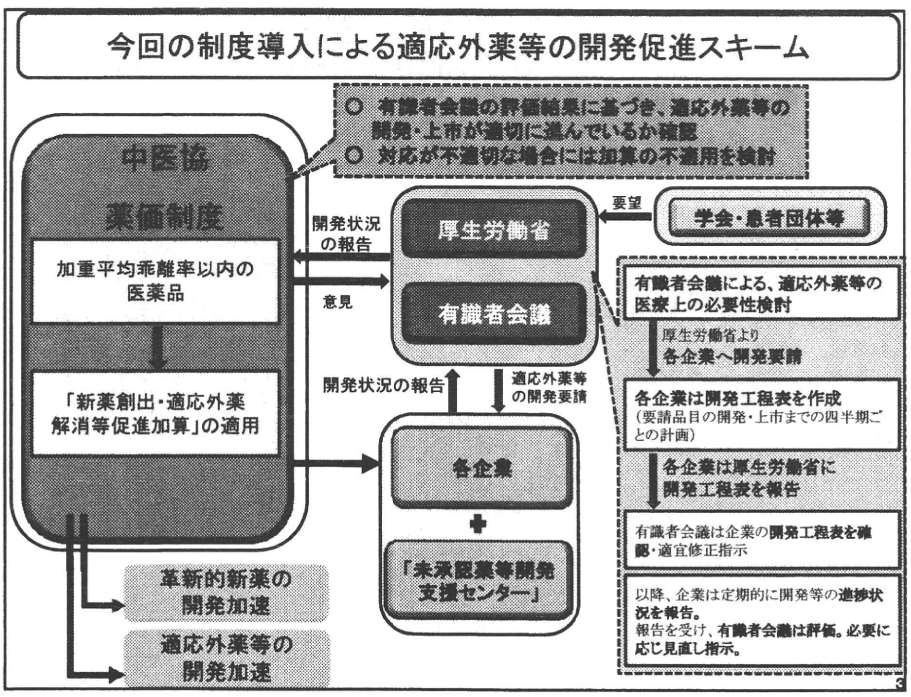
平成22年4月に独立法人化

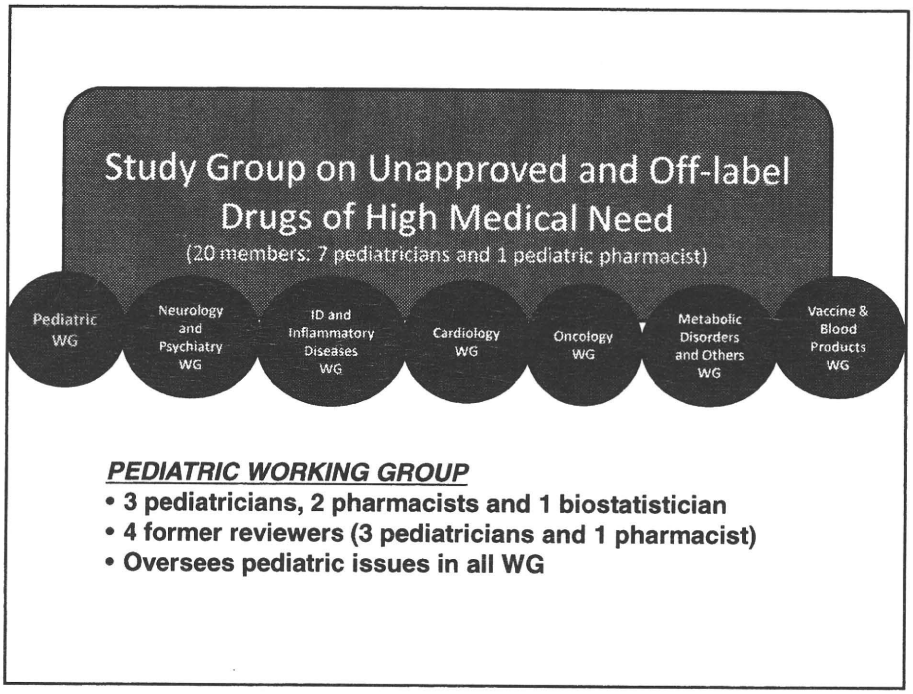


適応外薬・未承認薬解決のために新しいインセンティブの試行が、平成21年12月25日に決定しました。

平成22年度薬価改定で
「新薬創出・適応外薬解消等促進加算」
の試行導入（2年限定）が決定！

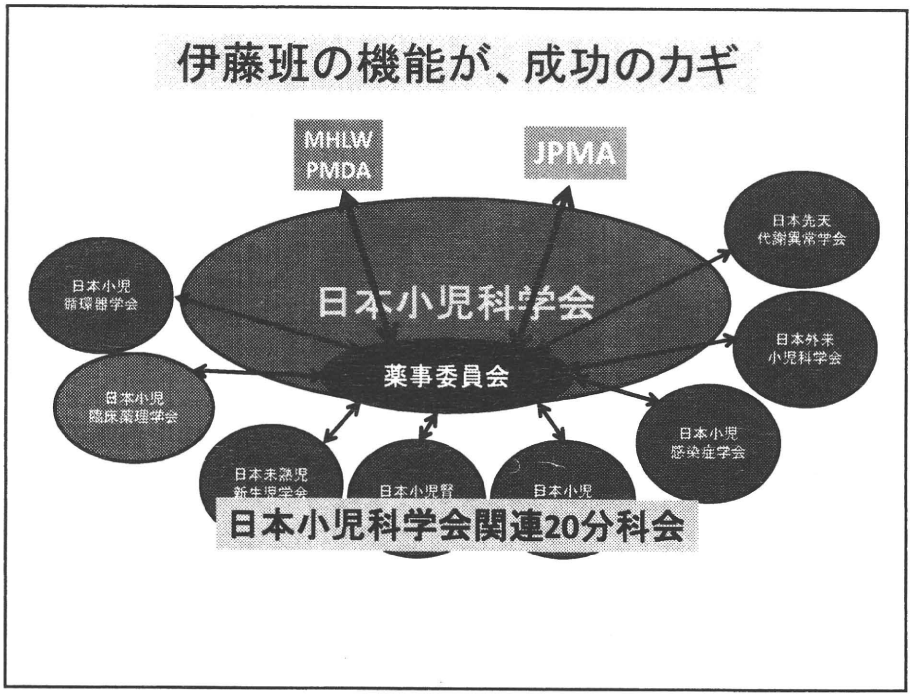

新薬創出・適応外薬解消等促進加算の対象となる新薬の薬価算定の例
薬価
要件：市場実勢価の乖離率が、全収載品の加重平均乖離率を超えない
先発→A円
当該加算の対象となった新薬の薬価
薬価改定猶予分
当該加算の対象とならなかった場合の新薬の薬価
（現行制度における新薬の薬価）
当該先発品の市場実勢価格による引下げ分
特例引き下げ分（4～6%）
新薬の薬価収載
新薬特許期間満了（後発品上市）又は薬価収載15年
新規後発品が上市された後の最初の薬価改定
時間


今回の制度導入による適応外薬等の開発促進スキーム
○ 有識者会議の評価結果に基づき、適応外薬等の開発・上市が適切に進んでいるか確認
○ 対応が不適切な場合には加算の不適用を検討
中医協
薬価制度
加重平均乖離率以内の医薬品
「新薬創出・適応外薬解消等促進加算」の適用
開発状況の報告
意見
厚生労働省
有識者会議
要望
学会・患者団体等
開発状況の報告
適応外薬等の開発要請
各企業
「未承認薬等開発支援センター」
革新的新薬の開発加速
適応外薬等の開発加速
有識者会議による、適応外薬等の医療上の必要性検討
厚生労働省より各企業へ開発要請
各企業は開発工程表を作成
（要請品目の開発・上市までの四半期ごとの計画）
各企業は厚生労働省に開発工程表を報告
有識者会議は企業の開発工程表を確認・適宜修正指示
以降、企業は定期的に開発等の進捗状況を報告。
報告を受け、有識者会議は評価。必要に応じ見直し指示。
3



PEDIATRIC WORKING GROUP

- **3 pediatricians, 2 pharmacists and 1 biostatistician**
- **4 former reviewers (3 pediatricians and 1 pharmacist)**
- **Oversees pediatric issues in all WG**



医療上の必要性の高い未承認薬・適応外薬検討会議の進行状況　平成22年11月9日時点

- 臨床上の必要性が高いと判断された未承認薬：60
- 臨床上の必要性が高いと判断された適応外薬：122
- 平成22年5月21日に企業に開発要請91件、開発企業募集17件
  - 開発要請を行った91件のうち
    - 公知申請が妥当：21件、すでに開発に着手：43件、治験の実施等が必要：14件、検討中：13件
  - 開発企業募集総計21件中17件に開発企業が決定
    - フェニル酪酸、ベタイン、カルグルミック散、ニチシノン、安息香酸ナトリウム・フェニル酢酸ナトリウム配合剤　等
  - 「適応外通知に則った承認」の事前評価済み
    - エルカルニチン：一次性及び二次性カルニチン欠乏症
    - メチルプレドニゾロン：ネフローゼ症候群
    - リュープロレリン：中枢性思春期早発症の最大用量を90μg/kg/4週→180 μg/kg/4週
    - ピンブラスチン：ランゲルハンス細胞組織球症　　等

小児医薬品開発はこれで進むか？

- 予算措置があって、やっと開発が決まった医薬品はすべてオーファンドラッグ
  - 今後さらに要望が出されるであろう、オーファンドラッグの開発の受け皿は十分か？
    - 企業に開発メリットがなければ、恐らく無理
- 現在のスキームは欧米の後追いでしかない
- 欧米では開発推進策が策定されている
  - 日本にも小児・希少疾病医薬品開発推進策が必要であろう

「医療上の必要性の高い未承認薬・適応外薬検討会議」を発展させて、EMAの小児委員会のような機能を持たせられないか

医療機器でも、医薬品と同様のスキームの検討が進行中
「ニーズの高い医療機器等の早期導入に関する検討会」

薬の粉末化 品質に不安

子ども用 病院や薬局で作業

医を創る

乏しい判断データ

手順の標準化が必要

今後手順の標準化と徹底が必要

粉砕等後の均一性、安定性に関する情報は、医薬品の承認時に取得すべき情報でないため、たとえ製薬企業が保有していても公開されない。

薬剤師の経験と勘に頼っている

平成21年から、国立成育医療センターでは製剤検討ラボを整備し、検討を始めました。
詳しくは「薬局」に連載されている「小児医療現場で起こっている危険」をご覧ください。

栗山 他:2009年第36回日本小児臨床薬理学会年会より改変

Pediatric Labeling Changes through February 25, 2011

This table highlights key pediatric information from the studies submitted in response to pediatric legislative initiatives (see below). Biologics have a solid dot (•) by the proper name. The table presents the most recent information first and it is searchable (e.g., Trade Name, Generic Name).

N=404

n= 368 with new pediatric studies; n=36 with no new pediatric studies (NNPS)

	Pediatric Labeling Date	Trade Name	Generic or Proper (Biologics•) Name	Indications Studied	Product Labeling	Labeling Changes	BPCA (B)/ PREA (P)/ Rule (R)	Sponsor	Pediatric Exclusivity Granted Date	NNPS
1.	1/30/2011	MENVEO	Meningococcal (Groups A, C, Y, and W-135) Oligosaccharide Diphtheria CRM197 Conjugate Vaccine•	Active immunization to prevent invasive meningococcal disease caused by *Neisseria meningitidis* serogroups A, C, Y and W-135		See Package Insert for new information on biologics	P	Novartis	NA	
2.	1/18/2011	Natroba Topical Suspension	spinosad	Treatment of head lice infestation in patients 4 years of age and older.		• Safety and effectiveness have been established in pediatric patients 4 years of age and older • Safety in pediatric patients < 4 years has not been established. • Not recommended in pediatric patients< 6 months because of the potential for increased systemic absorption • Natroba contains benzyl alcohol which has been associated with serious adverse reactions and death in neonates and low birth-weight infants. Premature and low-birth weight infants, as well as patients receiving high dosages, may be more likely to develop toxicity • Information on clinical trials, adverse reactions • New drug	P	ParaPRO	NA	
3.	12/22/2010	GARDASIL	Human Papillomavirus Quadrivalent (Types 6, 11, 16, 18) Vaccine, Recombinant•	Prevention of anal cancer and associated precancerous lesions caused by HPV types 16 and 18		See Package Insert for new information on biologics	P	Merck	NA	✓

	Pediatric Labeling Date	Trade Name	Generic or Proper (Biologics•) Name	Indications Studied	Product Labeling	Labeling Changes	BPCA (B)/ PREA (P)/ Rule (R)	Sponsor	Pediatric Exclusivity Granted Date	N N P S
4.	12/21/2010	INOmax for Inhalation	nitric oxide	Prevention of bronchopulmonary dysplasia		• INOmax is not indicated for prevention of BPD in preterm neonates ≤ 34 weeks gestational age. • Efficacy for the prevention of BPD in preterm infants was not established in three ldouble-blind, placebo-controlled clinical trials in a total of 2,149 preterm infants • Information on clinical trials, adverse reactions	B	INO Therapeutics	11/2/2010	
5.	12/15/2010	Uroxatral extended-release tablets	alfuzosin	Elevated detrusor leak point pressure of neurologic origin	Labeling	• Uroxatral is not indicated for use in the pediatric population • Efficacy was not demonstrated in a randomized, double-blind, placebo-controlled, efficacy and safety trial conducted in 172 patients ages 2 to 16 years using pediatric formulations	B	sanofi-aventis	9/7/2010	
6.	11/19/2010	Moxeza ophthalmic solution	moxifloxacin hydrochloride	Bacterial conjunctivitis	Labeling	• Approved for use in patients 4 months and older • The safety and effectiveness have not been established in patients <4 months of age • There is no evidence that the ophthalmic administration of moxifloxacin has any effect on weight bearing joints, even though oral administration of some quinolones has been shown to cause arthropathy in immature animals • Information on clinical study, adverse reactions • New dosage form	P	Alcon	NA	
7.	11/10/2010	Vyvanse	lisdexamfetamine	ADHD	Labeling	• Expanded indication to include adolescent patients ages13-17 years; previously approved for use in 6-12 years • Most common adverse reactions were decreased appetite, insomnia, and decreased weight • Information on clinical trial, adverse reactions	P	Shire	NA	
8.	11/2/2010	Ofirmev Injection	acetaminophen	Management of mild-to-moderate pain, for the management of moderate-to-severe pain with adjunctive opioid analgesics, and for the reduction of fever	Labeling	• The safety and effectiveness of Ofirmev for the treatment of acute pain and fever in pediatric patients ages 2 years and older is supported by evidence from adequate and well-controlled studies of Ofirmev in adults. Additional safety and PK data was collected in 355 from premature neonates to adolescents. • The effectiveness of Ofirmev for the treatment of acute pain and fever has not been studied in pediatric patients < 2 years of age.	P	Cadence Pharms	NA	

	Pediatric Labeling Date	Trade Name	Generic or Proper (Biologics•) Name	Indications Studied	Product Labeling	Labeling Changes	BPCA (B)/ PREA (P)/ Rule (R)	Sponsor	Pediatric Exclusivity Granted Date	N N P S
						• The PK exposure of Ofirmev observed in children and adolescents is similar to adults, but higher in neonates and infants. Dosing simulations from PK data in infants and neonates suggest that dose reductions of 33% in infants 1 month to < 2 years of age, and 50% in neonates up to 28 days, with a minimum dosing interval of 6 hours, will produce a PK exposure similar to that observed in children age 2 years and older • Most common adverse reactions in pediatric patients were nausea, vomiting, constipation, pruritus, agitation, and atelectasis. • Information on dosing, clinical studies, adverse reactions and PK parameters • New dosage form and route of administration				
9.	10/21/2010	Lo Loestrin Fe	norethindrone acetate/ ethinyl estradiol	Prevention of pregnancy	Labeling	• Safety and efficacy have been established in women of reproductive age. Safety and efficacy are expected to be the same for postpubertal adolescents <18 years and for users ≥18 years • Use before menarche is not indicated • New dose and dosing regimen	P	Warner Chilcott	NA	✓
10.	10/5/2010	Aridol Powder for Inhalation	mannitol	Assessment of bronchial hyperresponsiveness in patients without clinically apparent asthma	Labeling	• New indication in patients 6 years and older • Efficacy assessed in a total of 246 children and adolescents 6 to 17 years in 2 clinical trials • Bronchial challenge testing should not be performed in children < 6 years due to their inability to provide reliable spirometric measurements • Adverse events similar to adults • Information on adverse events and clinical studies • New indication, dosage form, and route of administration	P	Pharmaxis	NA	
11.	9/28/2010	Kapvay Extended Release Tablets	clonidine	Treatment of attention deficit hyperactivity disorder (ADHD) as monotherapy and as adjunctive therapy to stimulant medications	Labeling	• New indication in children 6 years and older • Efficacy is based on 2 clinical trials in children and adolescents 6 -17 years • Kapvay has not been studied in children with ADHD < 6 years • Kapvay can cause dose related decreases in blood pressure and heart rate	P	Shionogi	NA	

	Pediatric Labeling Date	Trade Name	Generic or Proper (Biologics•) Name	Indications Studied	Product Labeling	Labeling Changes	BPCA (B)/ PREA (P)/ Rule (R)	Sponsor	Pediatric Exclusivity Granted Date	N N P S
						• Common adverse events reported in clinical trials included somnolence, fatigue, upper respiratory tract infection irritability, throat pain, insomnia, nightmares, emotional disorder. In fixed dose pediatric monotherapy study, 31% of patients treated with 0.4 mg/day and 38% treated with 0.2 mg/day vs 7% of placebo treated patients reported somnolence. • Kapvay is an extended-release tablet formulation of clonidine; therefore, it is not to be used interchangeably with the immediate-release formulation • Information on adverse events, and clinical trials • New indication				
12.	9/24/2010	Beyaz	drospirenone/ ethinyl estradiol	Prevention of pregnancy; premenstrual dysphoric disorder; moderate acne vulgaris ≥14 years who have achieved menarche; to raise folate levels in a pregnancy conceived while on or shortly after discontinuing the product	Labeling	• Safety and efficacy have been established in women of reproductive age. Safety and efficacy are expected to be the same for postpubertal adolescents <18 years and for users ≥18 years • Use before menarche is not indicated • New combination	P	Bayer	NA	✓
13.	9/8/2010	Protopam	pralidoxime	Treatment of poisoning due to organophosphates (e.g., nerve agents)	Labeling	• Expanded indication from adults to pediatrics • Efficacy extrapolated from adult population and supported by nonclinical studies, PK studies in adults and experience in the pediatric population • Information on IV and IM dosing, and adverse events	P	Baxter	NA	✓
14.	9/3/2010	Zyrtec Allergy Orally Disintegrating Tablets	cetirizine	Temporary relief of symptoms due to hay fever or other upper respiratory allergies		• Approved for use in 6 years and older • No clinical studies submitted • New dosage form	P	McNeil Consumer Healthcare	NA	✓

	Pediatric Labeling Date	Trade Name	Generic or Proper (Biologics•) Name	Indications Studied	Product Labeling	Labeling Changes	BPCA (B)/ PREA (P)/ Rule (R)	Sponsor	Pediatric Exclusivity Granted Date	N N P S
				OTC						
15.	8/27/2010	Augmentin XR	amoxicillin/clavulanate potassium	Community-acquired pneumonia or acute bacterial sinusitis	Labeling	• Expanded indication from adults to children weighing ≥ 40 kg who are able to swallow tablets • Use in children is supported by evidence from trials of adults with additional data from a pediatric PK study • Adverse events similar to adults • Information on dose, and PK parameters • Information added to Clinical Pharmacology and Pediatric Use	P	GlaxoSmithKline	NA	
16.	8/13/2010	ella	ulipristal acetate	Prevention of pregnancy following unprotected intercourse or a known or suspected contraceptive failure	Labeling	• Safety and efficacy have been established in women of reproductive age. Safety and efficacy are expected to be the same for post pubertal adolescents <18 years and for users 18 years and older. • Use of ella before menarche is not indicated • New drug	P	Laboratoire HRA Pharma	NA	✓
17.	7/28/2010	Lastacaft Ophthalmic Solution	alcaftadine	Prevention of itching associated with allergic conjunctivitis.	Labeling	• Safety and effectiveness in patients >2 years were established in controlled clinical trials • Safety and effectiveness in pediatric patients< 2 years have not been established • New drug	P	Vistakon Pharmaceuticals,	NA	
18.	6/29/2010	Daytrana	methylphenidate	ADHD	Labeling	• Expanded pediatric indication to include adolescent patients ages13-17 years • The most commonly reported adverse reactions in a trial in patients 13-17 years included appetite decreased, nausea, insomnia, weight decreased, dizziness, abdominal pain, and anorexia. The majority	P	Shire	NA	

	Pediatric Labeling Date	Trade Name	Generic or Proper (Biologics•) Name	Indications Studied	Product Labeling	Labeling Changes	BPCA (B)/ PREA (P)/ Rule (R)	Sponsor	Pediatric Exclusivity Granted Date	N N P S
						of patients had erythema at the application site • Information on PK parameters, Adverse Event profile and clinical studies				
19.	6/22/2010	Isopto Carpine	pilocarpine hydrochloride	Reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension; management of acute angle closure glaucoma; prevention of postoperative elevated IOP associated with laser surgery and induction of miosis	Labeling	• Safety and effectiveness in pediatric patients have been established • Not recommended in pediatric patients diagnosed with glaucoma due to anterior segment dysgenesis or uveitis • Caution is advised in pediatric patients with primary congenital glaucoma for control of IOP as cases of a paradoxical increase in IOP have been reported. • Adverse events similar to adults • New dosage form	P	Alcon	NA	✓
20.	6/22/2010	Dulera Inhalation Aerosol	mometasone furoate and formoterol fumarate	Asthma	Labeling	• Safety and effectiveness have been established in patients 12 years and older in 3 clinical studies • Safety and efficacy have not been established in children <12 years • Data from clinical trials suggest that LABA increase the risk of asthma-related hospitalization in pediatric and adolescent patients • Information on adverse events and clinical studies • New combination	P	Schering	NA	

	Pediatric Labeling Date	Trade Name	Generic or Proper (Biologics•) Name	Indications Studied	Product Labeling	Labeling Changes	BPCA (B)/ PREA (P)/ Rule (R)	Sponsor	Pediatric Exclusivity Granted Date	N N P S
21.	6/3/2010	Zylet	loteprednol etabonate and tobramycin	Eye lid inflammation	Labeling	• Efficacy was not demonstrated in a study of pediatric patients 0-6 years	P	Bausch and Lomb	NA	
22.	5/27/2010	Advil Congestion Relief	ibuprofen /phenylepherin e HCl	Temporary relief of symptoms associated with cold and flu		• Indicated for use in children 12 years and older • Approval and age range based on monograph for decongestants and previous studies for ibuprofen • Do not use in children < 12 years because this product contains too much medication for this age • New drug	P	Wyeth	NA	✓
23.	5/26/2010	Nasonex	mometasone	Nasal congestion associated with seasonal allergic rhinitis	Labeling	• New indication in pediatric patients 2 years and older • Safety and effectiveness evaluated in 3 clinical studies in 12 years and older. Use in pediatric patients 2 - 11 years is supported by data from other pediatric clinical studies • Safety and effectiveness for any use in patients < 2 years have not been established • Information on dosing, adverse reactions, and clinical studies in 12 years and older • New indication	P	Schering-Plough	NA	
24.	5/18/2010	Zymaxid	gatifloxacin	Bacterial conjunctivitis	Labeling	• Safety and effectiveness have been demonstrated in clinical trials for the treatment of bacterial conjunctivitis in pediatric patients 1 year and older • The safety and effectiveness in infants < 1year have not been established • Information on adverse reactions and clinical trials • New drug	P	Allergan	NA	

	Pediatric Labeling Date	Trade Name	Generic or Proper (Biologics•) Name	Indications Studied	Product Labeling	Labeling Changes	BPCA (B)/ PREA (P)/ Rule (R)	Sponsor	Pediatric Exclusivity Granted Date	N N P S
25.	5/13/2010	Taxotere	docetaxel	Solid Tumors	Labeling	• Efficacy in pediatric patients as monotherapy or in combination has not been established. • Taxotere has been studied in a total of 289 pediatric patients: 239 in 2 trials with monotherapy and 50 in combination treatment with cisplatin and 5-fluoruracil • The overall safety profile in pediatric patients receiving monotherapy or combination treatment was consistent with the safety profile in adults • Information on dosing, clinical trials and PK parameters	B	Sanofi-aventis	3/17/2010	
26.	5/7/2010	Omnaris	ciclesonide	Postmarketing study	Labeling	• Information on clinical study to assess effect of orally inhaled ciclesonide on growth	P	Sepracor	NA	
27.	5/6/2010	Natazia	estradiol valerate and estradiol valerate/dienogest	Prevention of pregnancy	Labeling	• Safety and efficacy have been established in women of reproductive age. Safety and efficacy for post pubertal adolescents < 18 are expected to be the same as for 18 years and older • Use of this product before menarche is not indicated • New drug	P	Bayer	NA	✓
28.	4/12/2010	Pancreaze	pancrelipase	Treatment of exocrine pancreatic insufficiency due to cystic fibrosis or other conditions	Labeling	• Safety and efficacy assessed in 2 studies that included patients 6-30 months and 8--17 years • Safety and efficacy for use in all pediatric age groups based on information from the literature and clinical experience with different formulations of pancrelipase containing the same active ingredient • High doses of pancreatic enzyme products have been associated with fibrosing colonopathy in children <12 years of age • Adverse reactions similar to adults • Capsule should be swallowed whole. For infants or patients unable to swallow intact	P	Ortho-McNeil-Janssen	NA	

	Pediatric Labeling Date	Trade Name	Generic or Proper (Biologics•) Name	Indications Studied	Product Labeling	Labeling Changes	BPCA (B)/ PREA (P)/ Rule (R)	Sponsor	Pediatric Exclusivity Granted Date	N N P S
						capsules, the contents may be sprinkled on soft acidic food such as applesauce • Information on dosing and clinical studies • Not interchangeable with other pancrelipase products • New drug				
29.	3/24/2010	Viread	tenofovir disoproxil fumarate	Treatment of HIV infection in combination with other antiretroviral agents	Labeling	• Expanded indication from adults to pediatric patients 12- <18 years • Safety and effectiveness in patients < 12 years have not been established • In a clinical study of HIV-1 infected adolescents bone effects were similar to adults • The adverse reactions in trial in adolescents were consistent with those observed in clinical trials in adults • Information on dosing in adolescents weighing ≥35 kg, adverse reactions, and PK parameters	B, P	Gilead	NA	
30.	3/17/2010	Differin Lotion	adapalene	Acne	Labeling	• Safety and effectiveness established in 2 clinical studies in patients 12 years and older • Safety and effectiveness in pediatric patients less than 12 years have not been established • New dosage form	P	Galderma	NA	
31.	3/17/2010	MultiHance Injection	gadobenate dimeglumine	Intravenous use in magnetic resonance imaging	Labeling	• Extended indication from adults to pediatric patients 2 years and older • Safety and effectiveness in pediatric patients less than 2 years have not been established • Patients less than 2 years may be at increased risk of nephrogenic systemic fibrosis related to gadolinium due to immature kidney function • Adverse events similar to adult patients • Information on adverse events, PK, and clinical studies	P	Bracco Diagnostics	NA	

	Pediatric Labeling Date	Trade Name	Generic or Proper (Biologics•) Name	Indications Studied	Product Labeling	Labeling Changes	BPCA (B)/ PREA (P)/ Rule (R)	Sponsor	Pediatric Exclusivity Granted Date	NNPS
						• New indication				
32.	2/24/2010	Prevnar 13	Pneumococcal 13-valent Conjugate Vaccine (Diphtheria CRM197 Protein) •	Active immunization for the prevention of invasive disease caused by Streptococcus pneumoniae serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F, and for the prevention of otitis media caused by serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F	Package Insert	See Package Insert for new information on biologics	P	Wyeth	NA	
33.	2/22/2010	TamiFlu	oseltamivir	Prophylaxis of influenza	Labeling	• Information on postmarketing clinical study in patients 1 to 12 years	P	Hoffmann-La Roche Inc.	NA	
34.	2/19/2010	MENVEO	Meningococcal (Groups A, C, Y, and W-135) Oligosaccharide Diphtheria CRM197 Conjugate Vaccine•	Active immunization to prevent invasive meningococcal disease caused by *Neisseria meningitidis* serogroups A, C, Y and W-135	Package Insert	See Package Insert for new information on biologics	P	Novartis	NA	

	Pediatric Labeling Date	Trade Name	Generic or Proper (Biologics•) Name	Indications Studied	Product Labeling	Labeling Changes	BPCA (B)/ PREA (P)/ Rule (R)	Sponsor	Pediatric Exclusivity Granted Date	N N P S
35.	2/4/2010	Benicar	olmesartan	Hypertension	Labeling	• Expanded indication from adults to pediatric patients 6 years and older • Information on preparation of an oral suspension • Adverse events similar to adult patients • Information on dosing, adverse reactions, pharmacokinetics, and clinical studies	B, P	Daiichi Sankyo	10/7/2009	
36.	1/29/2010	Lamictal XR	lamotrigine	Adjunctive therapy for Primary Generalized Tonic-Clonic seizures	Labeling	• New indication for adjunctive therapy for primary generalized tonic-clonic seizures in patients ≥ 13 years of age • Safety and effectiveness for any use in patients < 13 years have not been established • Information on dosing, adverse reactions, and clinical studies	P	GlaxoSmithKline	NA	
37.	1/25/2010	Sandostatin and Sandostatin LAR	octreotide	Weight loss due to hypothalamic obesity from cranial insult	Labeling Labeling	• Post-marketing reports of hypoxia, necrotizing enterocolitis, and death in children added to Pediatric Use. The relationship of these events to octreotide has not been established. • Pediatric Use subsection of Sandostatin labeling harmonized with Sandostatin LAR labeling	B	Novartis	1/12/2006	✓
38.	1/4/2010	Xolair	omalizumab	Moderate to severe persistent asthma who have a positive skin test or in vitro reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with inhaled corticosteroids.		• Safety and effectiveness were evaluated in 2 studies in 926 asthma patients 6 to <12 years of age. The risk-benefit assessment does not support use in patients 6 to <12 years considering the risk of anaphylaxis and malignancy seen in Xolair-treated patients ≥12 years and the modest efficacy of Xolair in the pivotal pediatric study • Studies in patients 0-5 years were not required due to safety concerns of anaphylaxis and malignancy • Information added to Pediatric Use	P	Genentech	NA	