NOVARTIS

Elidel® 1% cream

Composition
Active substance: Pimecrolimus
Excipients: Propylene glycol, benzyl alcohol as preservative; vehicle excipients.

Pharmaceutical form and quantity of active substance per unit
10 mg/g cream

Indications / Potential uses
Short-term and intermittent long-term treatment of mild to moderate atopic dermatitis in patients from 2 years of age as second-line therapy in situations where conventional treatment with emollients and topical corticosteroids cannot be given.

Dosage and Administration
Use in adults
Elidel should only be initiated by doctors experienced in topical treatment of atopic dermatitis.
Continuous long-term treatment should be avoided and application restricted to areas of skin that are affected (see **Warnings and Precautions**).
A thin layer of Elidel should be applied to the affected skin twice daily, then rubbed in gently and completely. Affected areas should be treated until complete clearance occurs. An oily cream or ointment without any active substance should be used instead of Elidel during flare-free intervals.
If there is no noticeable improvement within 6 weeks, or in the event of exacerbation, treatment with Elidel should be discontinued and an alternative therapeutic option considered.
The attending physician should tell patients to take appropriate steps to protect themselves from sunlight, for example by minimizing the duration of exposure to sunlight, using sunscreen products and wearing appropriate clothing to cover the skin (see **Warnings and Precautions** and **Interactions**).
Elidel may be used on all areas of skin, including the head, face and neck (but not on mucous membranes). It should not be applied under occlusion.
Emollients may be applied immediately after using Elidel 1% cream. However, after a bath or shower emollients should be applied before using Elidel 1% cream.

Paediatric use
For children (aged 2–11 years) and adolescents (aged 12–17 years) the dosing recommendations are the same as for adults.
Use of Elidel is not recommended in children under 2 years of age owing to the lack of sufficient data on its effect on the developing immune system.

Use in the elderly
Atopic dermatitis (eczema) is rarely observed in patients aged 65 years and over. Clinical studies with Elidel 1% cream did not include a sufficient number of patients in this age group to determine whether they respond differently from younger patients.

Contraindications
Hypersensitivity to pimecrolimus, tacrolimus or any of the excipients.

Warnings and Precautions
The safety of Elidel for long-term use has not been established.
Elidel acts as a calcineurin inhibitor. An increased incidence of benign and malignant neoplasms, including lymphoproliferative disorders, has been observed with long-term systemic use of other products of this substance class approved for use in transplantation. Systemic bioavailability is considerably lower with topical cutaneous application. However, even with this type of use the long-term safety of calcineurin inhibitors has not been demonstrated.
Although a causal relationship to topical treatment has not been established, there have been rare reports of malignancy (e.g. skin malignancy and lymphoma) in patients treated with topical calcineurin inhibitors, including Elidel (see **Adverse effects**).
The long-term effect on the local skin immune response and on the incidence of skin malignancies is unknown, and Elidel should therefore not be applied to potentially malignant or pre-malignant skin lesions.
Continuous long-term treatment with topical calcineurin inhibitors should be avoided and use restricted to affected areas of skin.
For reasons of safety, treatment with Elidel should be interrupted in patients newly infected with EBV until the infection has subsided, and the patients should be monitored for local lymphoproliferation.
Elidel must not be applied to areas affected by acute cutaneous viral infections (herpes simplex, chickenpox). Elidel has not been evaluated for its efficacy and safety in the treatment of clinically infected atopic dermatitis. Clinical infections at the affected sites should be cleared before treatment with Elidel is initiated.

Elidel should not be used in children under 2 years of age due to a lack of long-term data on its effect on the developing immune system.

The safety and efficacy of Elidel in immunocompromised patients have not been studied. Elidel is therefore not recommended in these patients.

In clinical studies, 14/1544 cases of lymphadenopathy (0.9%) were reported during use of Elidel. These cases of lymphadenopathy were usually related to infections and usually resolved following appropriate antibiotic therapy. Of these 14 cases, the majority had either a clear aetiology or were already resolving. The precise outcome is unknown in 4 cases because the lymphadenopathy had not resolved by the end of the study.
Patients who receive Elidel and who develop lymphadenopathy should have the aetiology of their lymphadenopathy investigated. In the absence of a clear aetiology for the lymphadenopathy, or in the presence of acute infectious mononucleosis, treatment with Elidel should be discontinued. Patients who develop lymphadenopathy should be monitored to ensure that the lymphadenopathy resolves.

Like all medicinal products, Elidel should be given at the lowest possible dose that still allows effective control of symptoms.

Elidel should not be used continuously, and long-term treatment should be intermittent. Patients should be instructed to end treatment when symptoms resolve and not to resume treatment until new symptoms occur. If there is no improvement in symptoms after 6 weeks, or if the patient's condition deteriorates, treatment with Elidel should be withdrawn and the patient reassessed.

Patients with atopic dermatitis are susceptible to superficial skin infections such as eczema herpeticum (Kaposi's varicelliform eruption). Treatment with Elidel may therefore be associated with an increased risk of herpes simplex infection or eczema herpeticum (recognizable by the rapid spread of vesicular and erosive lesions). If a herpes simplex infection occurs, treatment with Elidel should not be continued at the affected site until the viral infection has subsided.

Although bacterial skin infections were rarer in patients treated with Elidel than in those given placebo, the risk of such infections (impetigo) in patients with severe atopic dermatitis may be elevated during treatment with Elidel.

Elidel may cause mild and transient reactions, such as a feeling of warmth and/or a burning sensation, at the site of application. In the event of a pronounced skin reaction at the application site, the benefit-risk ratio of treatment should be reassessed.

Contact with the eyes and mucosa should be avoided. If the cream is accidentally applied to these areas, it should be carefully wiped off and/or washed off with water.
There have been no studies in patients on the use of Elidel under occlusive dressings. Occlusive dressings are not recommended.
The safety of Elidel has not been studied in patients with Netherton's syndrome and generalized erythroderma. Elidel is not recommended in patients with Netherton's syndrome or severely inflamed or damaged skin (e.g. erythroderma) due to the potential for increased systemic absorption of the active substance.
It is not known in what ways Elidel might alter skin reactions to damage by UV irradiation. The attending physician should therefore tell patients to take appropriate steps to protect themselves from sunlight during the course of treatment (using sunscreen products and wearing appropriate clothing to cover the skin). Patients should minimize or avoid exposure to natural or artificial sunlight (see **Interactions**, **Preclinical data**) even when no Elidel has been applied to the skin.
Elidel contains cetyl alcohol and stearyl alcohol, which may cause local cutaneous reactions. It also contains propylene glycol, which may cause skin irritation.

Interactions
Potential interactions between Elidel and other medicinal products have not been systematically studied.
Pimecrolimus is exclusively metabolized by CYP450 3A4. Based on its minimal extent of absorption, interactions between Elidel and systemically administered drugs are unlikely to occur.
Currently available data show that Elidel may be used concomitantly with antibiotics, antihistamines and (oral/nasal/inhaled) corticosteroids.
Based on the minimal extent of absorption, a potential systemic interaction with vaccination is unlikely to occur. However, this interaction has not been studied. It is therefore recommended that inoculation be carried out during treatment-free intervals in patients with extensive atopic dermatitis.
Concomitant application of other topical anti-inflammatory products, including corticosteroids, has not been studied. For this reason, Elidel should not be applied concomitantly with topical corticosteroids or other topical anti-inflammatory products.
There is no experience of concomitant use with other immunosuppressive therapies given for atopic dermatitis, such as UVA, PUVA, UVB, azathioprine or ciclosporin.
Elidel has no photocarcinogenic potential in animals. However, since the relevance of these findings to humans is not known, excessive exposure of the skin to ultraviolet light, e.g. from a solarium or treatment with PUVA, UVA or UVB, should be avoided during treatment with Elidel.

Pregnancy and Lactation
Pregnancy
Animal studies involving dermal application have not shown direct or indirect harmful effects with respect to pregnancy, embryonic/fetal development, parturition or postnatal development. Animal studies have shown a toxic effect of pimecrolimus on reproductive functions following systemic administration of clearly toxic doses; there have, in particular, been occurrences of delayed or incomplete ossification.
The use of Elidel during pregnancy has not been studied. The potential risk in humans is not known. Elidel 1% cream should therefore not be prescribed during pregnancy.

Lactation
Animal studies on milk excretion following topical application were not conducted. It is not known whether pimecrolimus is excreted in breast milk following topical application.
The product should therefore only be prescribed for breastfeeding women in exceptional cases. Application to the breast should be avoided in order to avoid accidental oral ingestion by the infant.

Effects on ability to drive and use machines
The effect of Elidel 1% cream on the ability to drive or use machines has not been studied.

Adverse effects
The most common adverse effects were application-site reactions, which were reported by approximately 19% of the patients treated with Elidel 1% cream and 16% of patients in the control group. These reactions generally occurred at the start of treatment, were mild/moderate in severity and were of short duration.
Frequency estimates (CIOMS): very common (> 1/10); common (> 1/100 to < 1/10); uncommon (> 1/1000 to < 1/100); rare (> 1/10 000 to < 1/1000); very rare (< 1/10 000), including isolated cases.
- Very common: Burning sensation at the site of application.
- Common: Application site reactions (irritation, pruritus and erythema), skin infections (folliculitis).
- Uncommon: Impetigo, aggravation of condition, herpes simplex, herpes simplex dermatitis (eczema herpeticum), herpes zoster, molluscum contagiosum, application site reactions such as rash, pain, paraesthesia, desquamation, dryness, oedema, skin papilloma, furuncles.
- Rare: Alcohol intolerance (in most cases flushing, rash, burning sensation, itching or swelling shortly after consumption of alcohol), allergic reactions (e.g. rash, urticaria, angioedema), skin discoloration (e.g. hypopigmentation, hyperpigmentation).
- Very rare: Anaphylactic reactions.
- Rare: Rare cases of malignancy – including cutaneous and other types of lymphoma – and skin cancers have been reported in patients using pimecrolimus cream, although no causal relationship has been established (see **Warnings and Precautions**).

Overdose
There has been no experience of overdose with Elidel 1% cream.
No incidents of accidental ingestion have been reported.

Properties and Actions
ATC code: D11AX15.

Mechanism of action
Mechanism of action / Pharmacodynamics
Pimecrolimus, a lipophilic ascomycin macrolactam derivative with anti-inflammatory properties, is a cell-selective inhibitor of the production and release of pro-inflammatory cytokines.
Pimecrolimus binds with high affinity to macrophilin-12 and inhibits the calcium-dependent phosphatase calcineurin. As a result, synthesis of inflammatory cytokines in T cells is blocked.
Pimecrolimus exhibits high anti-inflammatory activity in animal models of skin inflammation after topical and systemic administration. Unlike corticosteroids, pimecrolimus does not cause skin atrophy in pigs.
Following topical application in mice, a reduction of up to 50% in oxazolone-induced hyperplasia was observed in local draining lymph nodes. Topical pimecrolimus penetrates similarly into – but permeates much less through – human skin than do corticosteroids, indicating a low potential for systemic absorption.
A study involving single applications of pimecrolimus to the skin of mice showed that concentrations of pimecrolimus can be higher in the primary draining lymph nodes than in the blood (see **Data from animal studies** under **Pharmacokinetics**).
For information on drug activity following oral administration, see **Preclinical data.**
In conclusion, pimecrolimus has a skin-selective profile different from that of corticosteroids.

Clinical data
Short-term (acute) treatment in paediatric patients
Children and adolescents
Two 6 week vehicle-controlled studies were conducted, involving a total of 403 paediatric patients aged 2 to 17 years. Patients were treated twice daily with Elidel 1% cream. The data of both studies were pooled.

Infants
A similar 6 week study was conducted in 186 patients aged 3–23 months.

In these three 6 week studies, the efficacy results at endpoint were as follows:

		Children and adolescents			Infants		
Endpoint	Criteria	Elidel 1% (N = 267)	Vehicle (N = 136)	p-value	Elidel 1% (N = 123)	Vehicle (N = 63)	p-value
IGA*:	Clear or almost clear[1]	34.8%	18.4%	< 0.001	54.5%	23.8%	< 0.001
IGA* ♦:	Improvement[2]	59.9%	33%	Not done	68%	40%	Not done
Pruritus ♦:	Absent or mild	56.6%	33.8%	< 0.001	72.4%	33.3%	< 0.001
EASI° ♦:	Overall (mean % change)[3]	–43.6	–0.7	< 0.001	–61.8	+7.35	< 0.001
EASI° ♦:	Head/Neck (mean % change)[3]	–61.1	+0.6	< 0.001	–74.0	+31.48	< 0.001

* Investigators Global Assessment
° Eczema Area Severity Index (EASI): mean % change in clinical signs (erythema, infiltration, excoriation, lichenification) and body surface area involved
♦ Secondary endpoint
1: p-value based on CMH test, stratified by centre
2: Improvement = lower IGA than at baseline
3: p-value based on ANCOVA model of EASI at Day 43 endpoint, with centre and treatment as factors and baseline (Day 1) EASI as covariate

A significant improvement in pruritus was observed within the first week of treatment in 44% of the children and adolescents and in 70% of the infants.

Long-term treatment in paediatric patients

Two double-blind studies of long-term management of atopic dermatitis were undertaken in 713 children and adolescents (2–17 years) and 251 infants (3–23 months). Elidel 1% cream was evaluated as pharmacologically active foundation therapy.

The study medication (Elidel 1% cream or vehicle) was used at the first sign of itching and redness to prevent acute flares of atopic dermatitis. Treatment with a medium potency corticosteroid was initiated only in the event of a flare of severe disease not adequately controlled by the study medication. Treatment with the study medication was discontinued as soon as corticosteroid therapy began.

Both studies showed a significant reduction in the incidence of flares ($p < 0.001$) during treatment with Elidel 1% cream. The efficacy of treatment with Elidel was also shown to be greater in all secondary target parameters (Eczema Area Severity Index, IGA, patients' assessments), and pruritus was controlled within a week with Elidel. A larger number of patients treated with Elidel completed 6 months (children: 61% with Elidel vs 34% in the control group; infants: 70% with Elidel vs 33% in the control group) and 12 months (children: 51% with Elidel vs 28% in the control group; infants: 57% with Elidel vs 28% in the control group) with no flares.

Topical corticosteroid use was reduced with Elidel. More patients treated with Elidel did not use corticosteroids over the 12 month period (children: 57% with Elidel vs 32% in the control group; infants: 64% with Elidel vs 35% in the control group). The efficacy of Elidel was maintained during the entire treatment period.

In addition, tolerability studies demonstrated that Elidel 1% cream does not cause photoirritation or contact sensitizing, and that it lacks any kind of phototoxic or photosensitizing potential.

The atrophogenic potential of Elidel 1% cream in humans was tested in comparison with medium and highly potent topical corticosteroids (betamethasone-17-valerate 0.1% cream, triamcinolone acetonide 0.1% cream) and vehicle in 16 healthy volunteers treated for 4 weeks. Both topical corticosteroids induced a significant reduction in skin thickness measured by echography as compared to Elidel 1% cream and vehicle, which did not induce any reduction in skin thickness.

Pharmacokinetics

Data from animal studies

The bioavailability of pimecrolimus in minipigs following a single dermal dose (applied for 22 hours under semi-occlusion) was about 0.03%. The amount of active substance-related material in the skin at the application site (almost exclusively unchanged pimecrolimus) remained practically constant for 10 days.

A study involving single applications of pimecrolimus to the skin of mice showed that 24 hours after application the concentration of pimecrolimus can be higher in the primary draining lymph nodes (148 ng/g) than in the blood (18 ng/ml). No results are available from pharmacokinetic studies involving repeated application.

Data from human studies

Absorption in adults

Systemic exposure to pimecrolimus was investigated in 12 adults with atopic dermatitis who were treated with Elidel twice daily for 3 weeks. The affected body surface area (BSA) ranged from 15% to 59%. 77.5% of pimecrolimus blood concentrations were below 0.5 ng/ml and 99.8% of the total samples were below 1 ng/ml.

The highest pimecrolimus blood concentration was 1.4 ng/ml in one patient.

The concentrations reached in locally involved lymph nodes were never determined in patients.

In 40 adult patients with an initially affected BSA of 14–62% who were treated with Elidel for 1 year, 98% of pimecrolimus blood concentrations were lower than 0.5 ng/ml. A maximum blood concentration of 0.8 ng/ml was measured in only 2 patients in week 6 of treatment. During the 12 months of treatment no increase in blood concentrations was observed in any patient. In 8 adult atopic dermatitis patients for whom AUC was quantifiable, $AUC_{(0\text{-}12h)}$ values ranged from 2.5 to 11.4 ng×h/ml.

Absorption in children

Systemic exposure to pimecrolimus was investigated in 58 paediatric patients aged 3 months to 14 years. The affected BSA ranged from 10 to 92%. These patients were treated with Elidel twice daily for 3 weeks, and 5 of them were treated for up to one year on an "as needed" basis.

The blood concentrations were consistently low, regardless of the extent of skin lesions or the duration of therapy. They were on the same order of magnitude as those in adult patients. Approximately 60% of pimecrolimus blood concentrations were below 0.5 ng/ml and 97% of all samples were below 2 ng/ml. The highest blood concentrations, measured in two paediatric patients (aged 8 months and 14 years), were 2 ng/ml.

The concentrations reached in locally involved lymph nodes were never determined in children.

In infants (3 to 23 months old), the highest blood concentration measured was 2.6 ng/ml in one patient. In the five children treated for 1 year, blood concentrations were consistently low (the maximum blood concentration measured was 1.94 ng/ml in 1 patient). There was no increase in blood concentration over time in any patient during the 12 months of treatment.

In 8 paediatric patients aged 2–14 years, $AUC_{(0\text{-}12h)}$ ranged from 5.4 to 18.8 ng×h/ml. AUC ranges observed in patients with < 40% BSA affected at baseline were comparable to those in patients with ≥ 40% BSA affected. The maximum BSA treated was 92% in clinical pharmacology studies and 100% in phase III clinical studies.

Distribution, metabolism and excretion

Pimecrolimus blood levels are very low following topical administration. For this reason, pimecrolimus metabolism could not be investigated following topical administration.

Following oral administration of a single dose of radiolabelled pimecrolimus in healthy subjects, unchanged pimecrolimus was the major active substance-related component in blood and there were numerous minor metabolites of moderate polarity that were classified as products of O-demethylation and oxygenation. Only cytochrome P450 3A4 is involved in metabolism.

Active substance-related radioactivity was excreted principally via the faeces (78.4%) and only a small fraction (2.5%) was recovered in the urine. Mean recovery of radioactivity was 80.9%. Unchanged active substance was not detected in the urine and less than 1% of radioactivity in the faeces was accounted for by unchanged pimecrolimus.

No metabolism of Elidel was observed *in vitro* in human skin.

Preclinical data

Toxicity studies after dermal application

A variety of preclinical safety studies were conducted with pimecrolimus cream formulations in several animal species. There was no evidence of irritation, photosensitization or other sensitization of skin, or local or systemic toxicity.

In a 2 year dermal carcinogenicity study in rats using Elidel 1% cream, no cutaneous or systemic carcinogenic effects were observed, even with the maximum practicable dose of 10 mg/kg/day, or 110 mg/m²/day.

The maximum dose corresponds to a mean $AUC_{(0\text{-}24h)}$ of 125 ng×h/ml, which is equivalent to 3.3 times the maximum exposure in children in clinical studies.

In a 104 week mouse dermal carcinogenicity study using pimecrolimus in an ethanolic solution, no increase in the incidence of neoplasms was observed in the skin or other organs up to the maximum dose of 200 µg/mouse, or 12 mg/m²/day.

In a similar 52 week mouse dermal carcinogenicity study using pimecrolimus in an ethanolic solution, no increase in the incidence of neoplasms was observed. Concentrations of pimecrolimus in mesenteric lymph nodes were 2–6 times higher than in the blood. Concentrations in the primary draining lymph nodes were not investigated in this study.

An increase in lymphoproliferative disturbances – such as those that have also occurred following long-term systemic administration of other calcineurin inhibitors in both animals and humans – was observed in mice undergoing long-term topical application of pimecrolimus in an ethanolic solution resulting in high systemic exposure.

In a dermal photocarcinogenicity study in hairless mice given Elidel 1% cream, as compared with vehicle, no photocarcinogenic effect occurred at doses up to the maximum of 10 mg/kg/day, or 30 mg/m²/day. Use of vehicle in the animals led to a 30% reduction in the latency period prior to the occurrence of skin tumours, as compared with untreated controls.

In dermal reproduction studies, no maternal or fetal toxicity was observed for doses up to the maximum practicable ones, i.e. 10 mg/kg/day, or 110 mg/m²/day, in rats and 10 mg/kg/day, or 36 mg/m²/day, in rabbits. In rabbits, the corresponding mean $AUC_{(0\text{-}24h)}$ was 24.8 ng×h/ml. AUC could not be calculated in rats.

Toxicity studies after oral administration

Certain adverse effects were not observed in clinical studies but were seen in animals with exposure to the active substance that was clearly in excess of normal maximum human exposure. It is thus likely that these adverse effects possess little relevance for clinical use. The effects in question are the following: slight maternal toxicity, oestrus cycle disturbances, post-implantation loss and reduction in litter size in reproduction studies in rats receiving oral doses up to 45 mg/kg/day, or 490 mg/m²/day, corresponding to an extrapolated mean $AUC_{(0\text{-}24h)}$ of 1448 ng×h/ml, or at least 63 times the maximum exposure observed in adult patients.

No effect on reproductive functions was observed at 10 mg/kg/day, or 110 mg/m²/day, corresponding to an extrapolated mean $AUC_{(0\text{-}24h)}$ of 465 ng×h/ml, or at least 20 times the maximum exposure observed in adult patients. In an oral reproduction study in rabbits, embryotoxic effects based on maternal toxicity, such as delayed or incomplete ossification, were observed at pimecrolimus blood concentrations 40 times higher, and $AUC_{(0\text{-}24h)}$ results 21 times higher, than the maximum values recorded in clinical studies following topical application in atopic dermatitis patients.

In an oral carcinogenicity study in mice given 45 mg/kg/day, or 135 mg/m²/day – corresponding to a mean $AUC_{(0\text{-}24h)}$ of 9821 ng×h/ml, or at least 258 times the maximum exposure observed in children in clinical studies – the incidence of lymphomas associated with signs of immunosuppression was 13% higher than in control animals. No increased incidence of lymphomas or discernible effects on the immune system were noted at 15 mg/kg/day, or 45 mg/m²/day, corresponding to a mean $AUC_{(0\text{-}24h)}$ of 5059 ng×h/ml, or 133 times the maximum exposure observed in children in clinical studies. In an oral carcinogenicity study in rats, no carcinogenic potential was observed up to a dose of 10 mg/kg/day, or 110 mg/m²/day, which is above the maximum tolerated dose and corresponds to an $AUC_{(0\text{-}24h)}$ of 1550 ng×h/ml, or 41 times the maximum exposure observed in children in clinical studies.

In a 39 week oral toxicity study in monkeys, a dose-dependent immunosuppression-induced lymphoproliferative disturbance associated with lymphocryptovirus and other opportunistic infections was observed at doses of 15–120 mg/kg/day. The dose of 15 mg/kg/day corresponds to a mean $AUC_{(0\text{-}24)}$ of 1193 ng×h/ml, or 31 times the maximum exposure observed in paediatric patients in clinical studies. At 45 mg/kg/day this lymphoproliferative disturbance was associated with mortality, reduced food intake, weight loss and pathological changes resulting from substance-related immunosuppression.

In the group receiving 120 mg/kg/day partial to complete reversibility was observed following discontinuation of dosing.

The limited data from this study show pimecrolimus concentrations to be higher in certain tissues than in the blood. This is in keeping with findings in rodents and with the known physical and chemical properties of pimecrolimus.

A battery of *in vitro* and *in vivo* genotoxicity tests – including Ames assay, mouse lymphoma L5178Y assay, chromosome aberration test in V79 Chinese hamster cells, and mouse micronucleus test – revealed no evidence that the active substance possesses mutagenic or clastogenic potential.

Other information

Shelf-life

This medication should not be used after the expiry date shown on the pack.

Special precautions for storage

See folding box.

After the tube is opened, its contents must be used within 12 months.

Pack sizes

Country specific pack sizes.

Manufacturer

See folding box.

Information last revised

November 2006

Approval date (text)

2 February 2007

® = registered trademark

Novartis Pharma AG, Basle, Switzerland

This is a medicament

- A medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are experts in medicine, its benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.

Keep medicaments out of reach of children

Council of Arab Health Ministers
Union of Arab Pharmacists

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