Kantonsspital St.Gallen

Kategorisierung von Studien

Zusatzinformationen

Inhalt

Fallbeispiel 2

Fluoxetin

Behavioral Activation Therapy

ICD 10 coding for depression

Fluoxetin Sandoz®

SANDOZ

Zusammensetzung

Wirkstoff: Fluoxetinum hydrochloridum ut fluoxetini hydrochloridum.

Hilfsstoffe

Kapseln: Color E 132, E 104; excipiens pro capsula.

Dispergierbare Tabletten: Excipiens pro compresso.

Galenische Form und Wirkstoffmenge pro Einheit

Kapseln

1 Kapsel enthält 20 mg Fluoxetinum ut fluoxetini hydrochloridum.

Dispergierbare Tabletten (teilbar)

1 dispergierbare Tablette enthält 20 mg Fluoxetinum ut fluoxetini hydrochloridum.

Indikationen/Anwendungsmöglichkeiten

Fluoxetin ist zur Behandlung von Depressionen unterschiedlicher Genese und Bulimia nervosa geeignet.

Dosierung/Anwendung

Depression

Die empfohlene Tagesdosis beträgt 20 mg Fluoxetin.

Obwohl Fluoxetin in klinischen Prüfungen bis zu 80 mg/Tag gegeben wurde, war der klinische Effekt bei 20 mg/Tag mit dem bei der höheren Dosierung vergleichbar. Falls in Einzelfällen erforderlich, kann die Dosis nach einigen Wochen schrittweise (20 mg) erhöht werden. Die Höchstdosis beträgt 80 mg Fluoxetin pro Tag.

Überschreitet die Tagesdosis 20 mg, so sollte sie während des Tages verteilt (z.B. morgens und abends) werden.

In speziellen Fällen (siehe unten) kann zur Dosisreduktion die Verabreichungsfrequenz reduziert werden, z.B. 20 mg jeden 2. Tag.

Bulimia nervosa

Die empfohlene Dosis beträgt 60 mg pro Tag.

Korrekte Art der Einnahme

Fluoxetin kann unabhängig von der Nahrung eingenommen werden.

Die dispergierbaren Tabletten (teilbar) können entweder direkt, ganz oder als Hälfte, oder dispergiert in ca. 100 ml Wasser, eingenommen werden.

Spezielle Dosierungsanweisungen

Eine Behandlung von Kindern und Jugendlichen unter 18 Jahren wird nicht empfohlen (siehe «Warnhinweise und Vorsichtsmassnahmen»).

Bei älteren Patienten und Patienten mit geringem Körpergewicht sollten 60 mg Fluoxetin pro Tag nicht überschritten werden; es werden niedrigere Dosen empfohlen.

Niereninsuffizienz: Bei Niereninsuffizienz kommt es unter mehrfacher Verabreichung von Fluoxetin zu einer Kumulation, welche im Allgemeinen eine Dosisanpassung erfordert.

Leberinsuffizienz: Aufgrund des verlängerten Metabolismus von Fluoxetin muss die vorgesehene Dosis reduziert werden. Das heisst z.B. 20 mg jeden 2. Tag.

Komedikation: Eine tiefere oder weniger häufige Dosis sollte in Betracht gezogen werden bei Patienten, welche mehrere Arzneimittel einnehmen.

Absetzsymptome bei Beendigung der Behandlung mit einem SSRI: Bei abruptem Absetzen der Behandlung mit SSRI sind Entzugssymptome mitgeteilt worden, wenn auch die verfügbaren Befunde nicht darauf hindeuten, dass dies auf Abhängigkeit zurückzuführen ist. Zu den häufigen Symptomen zählen Schwindel, Schlafstörungen, Parästhesien, Kopfschmerzen, Angst und Übelkeit; die Mehrzahl dieser Reaktionen ist leicht und selbstbegrenzend. Das Absetzen von Fluoxetin Sandoz war assoziiert mit solchen Symptomen. Daher soll bei Beendigung einer Behandlung mit Fluoxetin Sandoz die Dosis schrittweise reduziert werden, um das Risiko von Absetzerscheinungen zu verringern (siehe auch «Warnhinweise und Vorsichtsmassnahmen:

Absetzreaktionen bei Beendigung einer Behandlung mit einem Serotoninwiederaufnahmehemmer»).

Kontraindikationen

Überempfindlichkeit gegenüber Fluoxetin oder einem der in Fluoxetin Sandoz enthaltenen Hilfsstoffe. Bei akuten manischen Zuständen sollte eine Therapie mit Fluoxetin nicht initiiert werden.

MAO-Hemmer (irreversible und reversible): Die gemeinsame Verwendung von Fluoxetin und MAO-Hemmern muss vermieden werden. Bei gemeinsamer Gabe von Fluoxetin und MAO-Hemmern oder serotonergen Antidepressiva (wie z.B. Clomipramin, Präparate mit *Hypericum perforatum*) wurde über schwerwiegende Reaktionen berichtet.

Zu den Symptomen einer Wechselwirkung mit einem MAO-Hemmer gehören: Hyperthermie, Muskelstarre, Myoklonus, Instabilität des autonomen Nervensystems mit möglicherweise schnellen Schwankungen von Puls und Atmung sowie Veränderungen des psychischen Zustandes einschliesslich Verwirrtheit, Reizbarkeit und extremer Agitiertheit fortschreitend bis zu Delirium und Koma.

Da Fluoxetin und sein aktiver Metabolit eine lange Halbwertszeit aufweisen, sollte zumindest ein Abstand von 5 Wochen (ca. 5 Halbwertszeiten von Norfluoxetin) zwischen dem Absetzen von Fluoxetin Sandoz und dem Beginn der Therapie mit MAO-Hemmern eingehalten werden. Die Verabreichung von MAO-Hemmern innerhalb von 5 Wochen nach dem Absetzen von Fluoxetin Sandoz kann das Risiko von schweren Nebenwirkungen erhöhen. Todesfälle wurden berichtet, nachdem MAO-Hemmer kurzfristig nach dem Absetzen von Fluoxetin Sandoz eingenommen wurden.

Falls Fluoxetin chronisch und/oder in hoher Dosierung verschrieben wird, sollte ein längeres Intervall in Betracht gezogen werden.

Die Behandlung mit Fluoxetin darf frühestens 2 Wochen nach Absetzen eines irreversiblen MAO-Hemmers oder einen Tag nach Absetzen eines reversiblen MAO-A-Hemmers beginnen.

Warnhinweise und Vorsichtsmassnahmen

Bei einer Depression besteht ein erhöhtes Risiko für Suizidgedanken, Selbstverletzungen und Suizid (oder mit Suizidversuch zusammenhängenden Ereignissen). Das Risiko bleibt bestehen, bis es zu einer vollständigen Remission kommt. Ein erhöhtes Risiko suizidaler Verhaltensweisen kann auch mit anderen psychiatrischen Erkrankungen assoziiert sein, für deren Therapie Fluoxetin Sandoz eingesetzt wird.

Eine Behandlung von Kindern und Jugendlichen unter 18 Jahren mit Fluoxetin Sandoz wird nicht empfohlen, da suizidale Verhaltensweisen (Suizidversuch und Suizidgedanken) sowie Feindseligkeit (vorwiegend Aggressivität, oppositionelles Verhalten und Wut) in klinischen Studien häufiger bei mit Antidepressiva behandelten Kindern und Jugendlichen beobachtet wurden, als bei denen, die mit Placebo behandelt wurden.

Obwohl ein kausaler Zusammenhang von Fluoxetin Sandoz und dem Auftreten solcher Ereignisse bisher nicht nachgewiesen werden konnte, ergaben gepoolte Auswertungen von Studiendaten, dass suizidale Gedanken und/oder Verhaltensweisen im Vergleich zu Placebo bei Kindern und jungen Erwachsenen (im Alter <25 Jahre) unter Antidepressiva erhöht waren. Einem durch die Therapie begründeten Suizidrisiko steht das bekannte Risiko einer nicht ausreichend therapierten Depression gegenüber.

Begleitend zur Pharmakotherapie sollten Patienten engmaschig überwacht werden. Unabhängig vom Alter der Patienten sollten Ärzte ihre Patienten ermuntern, das Auftreten von deprimierenden Gedanken oder Gefühlen jederzeit mit dem Arzt zu besprechen.

Aus einer Analyse von kontrollierten Studien, in welche Erwachsene mit einer depressiven Episode nach ICD-10 Klassifikation (bzw. Major Depression Disorder MDD, nach DSM-IV Klassifikation) eingeschlossen worden waren, ergaben sich folgende Risikofaktoren für eine Suizidalität unter Placebo und Fluoxetin:

Vor Therapiebeginn:

– steigender Schweregrad der Depression;

– bestehende Suizidgedanken.

Während der Therapie:

– Verschlechterung der Depression;

– Entwicklung einer Insomnie (Schlaflosigkeit).

Eine schwerwiegende psychomotorische Aktivierung (zum Beispiel Agitation, Akathisie [siehe weiter unten unter «Akathisie/psychomotorische Unruhe»], Panik) während der Therapie mit

Fluoxetin stellte ebenfalls einen Risikofaktor dar.

Werden solche Krankheitsbilder vor Therapiebeginn beobachtet oder treten diese während der Therapie auf, sollte eine verstärkte klinische Beobachtung oder die Umstellung der Therapie in Erwägung gezogen werden.

Eine Änderung des Therapieregimes einschliesslich einer möglichen Absetzung der Medikation sollte bei Patienten in Erwägung gezogen werden, deren Zustand sich stetig verschlechtert oder deren auftauchende Suizidgefährdung ausgeprägt ist, plötzlich einsetzt oder nicht zu den anfänglichen Symptomen des Patienten zählte. Die Patienten und die sie betreuenden Personen müssen auf das mögliche Auftreten von Suizidalität im Rahmen einer antidepressiven Therapie und auf die dringende Notwendigkeit, den behandelnden Arzt in solchen Fällen aufzusuchen, aufmerksam gemacht werden.

Auch nach Abbruch der Behandlung müssen die Patienten gut überwacht werden, da solche Symptome sowohl als Zeichen eines Entzugs oder eines beginnenden Rückfalls auftreten können.

Andere psychiatrische Diagnosen als eine Depression können ebenfalls mit einem erhöhten Risiko von Suizidverhalten einhergehen.

Solche psychiatrische Diagnosen können auch im Rahmen einer Depression auftreten. Deshalb müssen bei diesen Erkrankungen die gleichen Vorsichtsmassnahmen bezüglich Suizidrisiko wie bei einer Depression beachtet werden.

Um das Risiko einer Überdosis zu verringern, sollte eine möglichst geringe, aber patientengerechte Tabletten- bzw. Kapselmenge verschrieben werden.

Manie/Hypomanie

Bis zum Einsetzen der antidepressiven Wirkung (1–3 Wochen) sind die Patienten ausreichend zu beobachten, auf das Auftreten von manischen und hypomanischen Symptomen. Wie alle Antidepressiva muss Fluoxetin abgesetzt werden, wenn ein Patient in eine manische Phase kommt.

Bei Studien aus den USA mit Fluoxetin traten bei 0,1% der Patienten mit Depression und bei 0,7% aller Patienten hypomanische oder manische Zustände auf.

Blutungen

SSRIs und SNRIs, einschliesslich Fluoxetin, können das Blutungsrisiko, inklusive gynäkologischer und gastrointestinaler Blutungen, erhöhen (siehe «Unerwünschte Wirkungen»). Daher ist Vorsicht geboten bei Patienten, die Fluoxetin zusammen mit Antikoagulantien und/oder Arzneimitteln einnehmen, von denen bekannt ist, dass sie die Plättchenfunktion beeinflussen (z.B. NSAIDs, Acetylsalicylsäure, atypische Neuroleptika wie Clozapin, Phenothiazine, die meisten trizyklischen Antidepressiva) und bei Patienten mit bekannter Blutungsneigung. Im Zusammenhang mit SSRIs gibt es Berichte über Hautblutungen wie Ekchymose und Purpura. Während der Behandlung mit Fluoxetin wurde gelegentlich über Ekchymosen berichtet.

Kardiovaskuläre Probleme

Bei Patienten mit Herz- oder Blutdruckproblemen sollten die üblichen Vorsichtsmassnahmen eingehalten werden (siehe «Unerwünschte Wirkungen»).

Da eine QT-Zeit-Verlängerung bei Fluoxetin-Exposition unter bestimmten Umständen ein potentielles Risiko darstellen kann, ist Vorsicht geboten, wenn Fluoxetin bei Patienten angewendet wird mit Erkrankungen wie angeborenes Long-QT-Syndrom, erworbenes Long-QT-Syndrom (z.B. aufgrund gleichzeitiger Anwendung eines Arzneimittels, das die QT-Zeit verlängert), sowie bei positiver Familienanamnese für QT-Zeit-Verlängerung oder in anderen klinischen Situationen, die für Arrhythmien prädisponieren (z.B. Hypokaliämie oder Hypomagnesiämie) oder bei erhöhter Fluoxetin-Exposition (z.B. bei Leberfunktionsstörungen).

Interaktionen/Serotoninsyndrom

Für MAO-Hemmer siehe «Kontraindikationen». In Kombination mit anderen serotonergen Wirkstoffen wie Triptanen, Lithium, L-Tryptophan und/oder neuroleptischer Arzneimitteln kann es in seltenen Fällen zu einem Serotoninsyndrom kommen. Die Symptomatik äussert sich in typischen Symptomen wie: Hyperreflexie, Tremor, Myoklonie, Rigor, mentale Veränderungen wie Unruhe, Angst, Verwirrung, Halluzinationen, Reizbarkeit bis zu Delirium und Koma, sowie Tachykardie, Blutdruckschwankungen, Hyperthermie, Übelkeit, Erbrechen, Durchfall.

Akathisie/psychomotorische Unruhe

Die Anwendung von Fluoxetin Sandoz wurde mit der Entwicklung von Akathisien in Verbindung gebracht, die charakterisiert sind durch eine subjektiv unangenehme und als quälend erlebte Ruhelosigkeit und Notwendigkeit sich zu bewegen, oft zusammen mit einer Unfähigkeit still zu sitzen oder still zu stehen. Dies tritt am ehesten während der ersten Behandlungswochen auf. Für Patienten, bei denen solche Symptome auftreten, kann eine Dosiserhöhung schädlich sein.

Absetzreaktionen bei Beendigung einer Behandlung mit einem Serotoninwiederaufnahmehemmer

Absetzreaktionen treten bei einer Beendigung der Behandlung häufig auf, besonders wenn die Behandlung plötzlich abgebrochen wird (siehe «Unerwünschte Wirkungen»). In klinischen Prüfungen traten sowohl in der Fluoxetin Gruppe als auch in der Placebo Gruppe bei 60% der Patienten nach Absetzen der Behandlung Nebenwirkungen auf. Von diesen Nebenwirkungen waren 17% in der Fluoxetin Gruppe und 12% in der Placebo Gruppe schwerwiegend. Das Risiko von Absetzreaktionen kann von mehreren Faktoren abhängen, einschliesslich Dauer der Behandlung, Dosis und Geschwindigkeit der Dosisreduktion. Schwindelgefühl, Empfindungsstörungen (einschliesslich Parästhesien), Schlafstörungen (einschliesslich Schlaflosigkeit und intensiver Träume), Schwäche, Erregtheit oder Angst, Übelkeit und/oder Erbrechen, Zittern und Kopfschmerzen sind die am häufigsten berichteten Reaktionen. Im Allgemeinen sind diese Symptome leicht bis mässig schwer, bei einigen Patienten können sie schwerwiegend sein. Sie treten normalerweise innerhalb der ersten Tage nach Absetzen der Behandlung auf. Im Allgemeinen bilden sich diese Symptome von selbst zurück und klingen innerhalb von 2 Wochen ab. Bei einigen Personen können sie länger anhalten (2–3 Monate oder länger). Es wird daher empfohlen bei einer Beendigung der Behandlung mit Fluoxetin Sandoz die Dosis über einen Zeitraum von mehreren Wochen oder Monaten schrittweise zu reduzieren, entsprechend den Bedürfnissen des Patienten (siehe «Dosierung/Anwendung: Absetzsymptome bei Beendigung der Behandlung mit einem SSRI»).

Ausschlag

Seit der Einführung von Fluoxetinhydrochlorid sind bei Patienten mit Ausschlägen systemische Krankheitsfälle, die möglicherweise mit Vaskulitis in Verbindung stehen, beobachtet worden. Diese Fälle treten zwar nur selten auf, können aber durch ihren Einfluss auf Lunge, Nieren oder Leber ernsthafte Folgen haben. Berichten zufolge können diese systemischen Erkrankungen auch zum Tod führen. Es wurde über anaphylaktische Erscheinungen z.B. mit Bronchospasmus, angioneurotischen Ödemen und Urtikaria berichtet.

Beim Auftreten eines Ausschlages oder anderer möglicherweise allergischer Phänomene für welche keine andere Ursache identifiziert werden kann, sollte Fluoxetin abgesetzt werden.

Krampfanfälle

Krampfanfälle sind ein mögliches Risiko bei Antidepressiva. Daher sollte, wie bei anderen Antidepressiva, bei Patienten mit Krampfanfällen in der Vorgeschichte eine Behandlung mit Fluoxetin nur mit Vorsicht begonnen werden. Treten bei einem Patienten Krampfanfälle neu auf oder nimmt die Häufigkeit von Krampfanfällen zu, muss die Behandlung abgebrochen werden. Eine Behandlung mit Fluoxetin sollte bei Patienten mit instabilen Anfallsleiden/Epilepsie vermieden werden. Patienten mit einer gut eingestellten Epilepsie müssen sorgfältig überwacht werden.

Hyponatriämie

Fälle von Hyponatriämie (einige mit Natrium-Werten niedriger als 110 mmol/l) wurden berichtet. Die Mehrheit dieser Fälle fanden bei älteren Patienten und bei Patienten, welche mit Diuretika behandelt wurden, oder bei sonst Volumen-reduzierten Patienten statt (siehe «Unerwünschte Wirkungen»).

Glykämische Überwachung

Bei Patienten mit Diabetes mellitus trat Hypoglykämie während der Therapie mit Fluoxetin auf und entwickelte sich Hyperglykämie nach dessen Absetzung. Die Dosierung von Insulin und oraler Antidiabetika muss eventuell angepasst werden, wenn eine Fluoxetin-Therapie begonnen oder beendet wird.

Physische und psychische Abhängigkeit

Wie bei der Verabreichung anderer ZNS-wirksamer Arzneimittel sollten Ärzte bei Ihren Patienten sorgfältig die Möglichkeit einer allfälligen Vorgeschichte von Arzneimittelabhängigkeit abklären, solche Patienten überwachen und sie betreffend Zeichen eines allfälligen Missbrauchs von Fluoxetin Sandoz (z.B. Entwicklung einer Toleranz, Dosiserhöhung, übermässige Nachfrage nach dem Arzneimittel) beobachten.

Elektrokrampftherapie: siehe «Interaktionen».

Johanniskraut (Hypericum perforatum)

Unerwünschte Wirkungen können bei gleichzeitiger Anwendung von Serotonin-Wiederaufnahme-Hemmern und pflanzlichen Präparaten, welche Johanniskraut enthalten, auftreten. Insbesondere kann es zu einer Zunahme von serotonergen Wirkungen wie einem Serotoninsyndrom kommen.

Mydriasis

Es wurde über Fälle von Mydriasis im Zusammenhang mit Fluoxetin berichtet. Daher ist Vorsicht geboten bei der Verschreibung von Fluoxetin bei Patienten mit erhöhtem Augeninnendruck oder Patienten mit einem Risiko für ein akutes Engwinkelglaukom.

Wegen der langen Eliminationshalbwertszeiten der Muttersubstanz und ihrer Metaboliten spiegeln sich Dosisänderungen in den ersten Wochen nicht vollständig im Plasma wider, was die Endtitration einer evtl. zu verabreichenden Dosis und den eventuellen Abbruch der Therapie beeinträchtigt (siehe «Pharmakokinetik»). Die gleichen Überlegungen gelten auch für das mögliche Auftreten von Interaktionen.

Bei gleichzeitiger Therapie mit ZNS-wirksamen Substanzen ist Vorsicht bei der Dosierung geboten, da sich die gegenseitige Wirkung verstärken kann (siehe «Interaktionen»).

Da Fluoxetin stark an Plasmaproteine gebunden wird, kann die Gabe von Fluoxetin bei Patienten, die bereits ein anderes, ebenfalls stark an Plasmaproteine gebundenes Arzneimittel (z.B. orale Antikoagulantien, Digitoxin) einnehmen, zu einer Abweichung der Plasmakonzentrationen führen, die wiederum unerwünschte Reaktionen verursachen können (siehe «Interaktionen»).

Interaktionen

Die gleichzeitige Gabe von Fluoxetin mit anderen serotonergen Wirkstoffen (MAO-Inhibitoren, Triptane, L-Tryptophan, Lithium, trizyklische Antidepressiva, Präparate mit Johanniskraut u.a.) kann zu einem Serotoninsyndrom führen (siehe «Kontraindikationen» und «Warnhinweise und Vorsichtsmassnahmen»).

Arzneimittel metabolisiert durch Cytochrom P450 2D6 Isoenzym: Da Fluoxetin das Potential hat, das Cytochrom P450 2D6 Isoenzym zu inhibieren, sollte eine gleichzeitige bzw. eine innerhalb 5 Wochen nach einer Fluoxetin-Therapie erfolgende Medikation, welche vor allem durch das Enzym P450 2D6 metabolisiert wird (z.B. Imipramin, Desipramin, Risperidon, Venlafaxin, Haloperidol, Clozapin, Flecainid, Propafenon), insbesondere jene mit schmalem therapeutischem Index, einschleichend eingeleitet werden, oder es sollte eine niedrigere Dosierung gewählt werden.

Arzneimittel metabolisiert durch CYP3A4 oder CYP2C: Es wurden Änderungen des Blutspiegels von Alprazolam, Carbamazepin, Diazepam oder Phenytoin und in einigen Fällen Symptome von Toxizität beobachtet. Vorsichtigere Titrationsverläufe für das mitverschriebene Produkt und Überwachung des klinischen Status sollte in Betracht gezogen werden.

Proteinbindung: Da Fluoxetin stark an Plasmaprotein gebunden wird, kann die Einnahme von Fluoxetin zusätzlich zu einem anderen Arzneimittel, welches stark an Protein gebunden wird, die Plasmakonzentration jedes einzelnen dieser Arzneimittel ändern.

In einigen Fällen sind Interaktionen mit Digoxin beschrieben worden. Bei gleichzeitiger Verabreichung von Fluoxetin mit Digoxin empfiehlt es sich deshalb, den Digoxin-Spiegel zu überprüfen.

Warfarin und andere orale Antikoagulantien: Über geänderte anti-koagulierende Effekte (Laborwerte und/oder klinische Zeichen und Symptome) ohne klares Erscheinungsbild aber mit erhöhter Blutung wurde selten berichtet, wenn Fluoxetin zusammen mit Warfarin verabreicht wurde. Patienten, welche gleichzeitig ein Cumarinpräparat erhalten, sollten sorgfältig auf Koagulation überwacht werden, wenn eine Behandlung mit Fluoxetin begonnen oder beendet wird.

Elektrokonvulsive Therapie (ECT): Es gab Berichte von verlängerten epileptischen Anfällen bei Patienten auf ECT Behandlung unter Fluoxetin. Daher ist Vorsicht geboten.

Eliminationshalbwertszeit: Die langen Eliminationshalbwertszeiten von Fluoxetin und seines Hauptmetaboliten, Norfluoxetin können potentiell nach Absetzen von Fluoxetin Auswirkungen haben, wenn Arzneimittel verschrieben werden, welche Wechselwirkungen mit einer der Substanzen haben.

Tryptophan

Eine gleichzeitige Gabe von L-Tryptophan soll ebenfalls nicht erfolgen. Zu dem Risiko eines Serotoninsyndroms siehe «Warnhinweise und Vorsichtsmassnahmen». Von der gleichzeitigen Verabreichung wird daher abgeraten.

Zentraldämpfende Pharmaka

Zentraldämpfende Pharmaka können durch Fluoxetin Sandoz in ihrer Wirkung verstärkt werden. Des Weitern kann es zu einer Erhöhung des Plasmaspiegels anderer Antidepressiva bei Kombination mit Fluoxetin Sandoz kommen.

Lithium

Fluoxetin kann den Lithium-Spiegel erhöhen, er sollte daher häufiger kontrolliert werden, wenn beide Substanzen gleichzeitig verabreicht werden. Zu dem Risiko eines Serotoninsyndroms siehe «Warnhinweise und Vorsichtsmassnahmen».

Alkohol

Alkohol ist während der Behandlung zu meiden, obwohl es in speziellen Untersuchungen zu keiner Verstärkung der Alkoholwirkung durch Fluoxetin Sandoz gekommen ist.

Weitere, häufig begleitend eingenommene Substanzen

Bisher wurden bei gleichzeitiger Gabe von Alkohol, Barbituraten, anderen Beruhigungs- und Schlafmitteln und Thiazid-Diuretika, Blutdruck- und Schmerzmitteln, Schilddrüsenhormonen, Antihistaminika, Antibiotika, Cimetidin und anderen magensäurehemmenden Präparaten keine Wechselwirkungen beobachtet.

Johanniskraut (Hypericum perforatum)

Unerwünschte Wirkungen können bei gleichzeitiger Anwendung von Serotonin-Wiederaufnahme-Hemmern und pflanzlichen Präparaten, welche Johanniskraut enthalten, auftreten.

Schwangerschaft/Stillzeit

Schwangerschaft

Die Ergebnisse mehrerer epidemiologischer Studien zur Untersuchung des Risikos einer Fluoxetin Exposition in der Frühschwangerschaft waren inkonsistent und haben bislang keinen schlüssigen Beleg für ein erhöhtes Risiko kongenitaler Fehlbildungen erbracht. Jedoch weist eine Meta-Analyse auf ein mögliches Risiko kardiovaskulärer Defekte bei Kindern hin, deren Mütter im ersten Trimenon der Schwangerschaft Fluoxetin erhalten hatten, im Vergleich zu Kindern, deren Mütter kein Fluoxetin erhalten hatten.

Dennoch sollte Fluoxetin während der Schwangerschaft nur dann angewendet werden, wenn dies klar notwendig ist.

Speziell ist am Ende der Schwangerschaft Vorsicht geboten, da nach Einnahme von Fluoxetin bzw. anderen selektiven Serotonin-Wiederaufnahmehemmern bei einigen Neugeborenen folgende Absetzsymptome auftraten: Ess- und Schlafstörungen, Atmungsschwierigkeiten, Krampfanfälle, Temperaturschwankungen, Hypoglykämie, Tremor, Muskelhypotonie, Hyperreflexie, Emesis, vorübergehende Nervosität, abnormale Reizbarkeit und anhaltendes Weinen.

Neugeborene, deren Mütter in der späten Schwangerschaft selektive Serotonin-Wiederaufnahmehemmer (SSRI) einnahmen, können ein erhöhtes Risiko für eine persistierende pulmonale Hypertonie des Neugeborenen (PPHN) haben.

Stillzeit

Fluoxetin wird in menschliche Milch ausgeschieden. Falls eine Behandlung mit Fluoxetin Sandoz notwendig ist, soll abgestillt werden.

Wehen und Niederkunft

Der Effekt von Fluoxetin auf Wehen und Entbindung beim Mensch ist nicht bekannt.

Wirkung auf die Fahrtüchtigkeit und auf das Bedienen von Maschinen

Da unter Fluoxetin Sandoz über Schläfrigkeit und Schwindel berichtet wurde, ist Vorsicht geboten bei der Teilnahme am Strassenverkehr oder Bedienen von Maschinen, bis die individuelle Reaktion auf das Präparat ersichtlich ist. Die gleichzeitige Einnahme von Alkohol und oder anderen Arzneimitteln (siehe «Interaktionen») führt zu einer zusätzlichen Beeinträchtigung der Reaktionsbereitschaft und Psychomotorik. Die Patienten sollten auf diese Gefahr entsprechend aufmerksam gemacht werden.

Unerwünschte Wirkungen

Die am häufigsten berichteten Nebenwirkungen bei Patienten, die mit Fluoxetin behandelt wurden, waren Kopfschmerzen, Übelkeit, Schlaflosigkeit, Müdigkeit und Diarrhö.

Die nachfolgende Liste beinhaltet Nebenwirkungen aus klinischen Studien (n= 9297) sowie aus Spontanberichten. Einige dieser Nebenwirkungen entsprechen den Nebenwirkungen anderer SSRIs.

Häufigkeitseinteilung: Sehr häufig (≥1/10), häufig (≥1/100, <1/10) und gelegentlich (≥1/1000, <1/100), selten (≥1/10'000, <1/1000), sehr selten (<1/10'000).

Blut- und Lymphsystem

Selten: Thrombozytopenie, Leukopenie, Pancytopenie.

Erkrankungen des Immunsystems

Selten: anaphylaktische Reaktionen, Serumkrankheit.

Stoffwechsel- und Ernährungsstörungen

Häufig: verminderter Appetit (einschliesslich Anorexie), Gewichtsverlust.

Selten: Hyponatriämie.

Reversible inadäquate ADH Sekretion mit Hyponatriämie und Hirnödem (meist bei älteren

Patienten und Diuretikabehandlung) wurde berichtet.

Hypoglykämie wurde berichtet (siehe «Warnhinweise und Vorsichtsmassnahmen»).

Hypokaliämie wurde berichtet.

Psychiatrische Erkrankungen

Sehr häufig: Schlaflosigkeit (15,0%).

Häufig: Angst, Nervosität, Unruhe, Anspannung, Libidoverminderung (einschliesslich Libidoverlust), Schlafstörungen, abnormale Träume (einschliesslich Albträume).

Gelegentlich: Depersonalisation, gesteigerte Stimmung, euphorische Stimmung, abnormale Gedanken, abnormaler Orgasmus (einschliesslich Anorgasmie), Zähneknirschen.

Selten: manische/hypomanische Reaktion, Halluzinationen, Agitiertheit.

Verwirrtheit wurde berichtet.

Erkrankungen des Nervensystems

Sehr häufig: Kopfschmerzen (19,9%).

Häufig: Aufmerksamkeitsstörung, Schwindel, Geschmacksstörungen, Lethargie, Schläfrigkeit (einschliesslich Hypersomnie und Sedation), Tremor.

Gelegentlich: psychomotorische Hyperaktivität, Dyskinesie, Ataxie, Gleichgewichtsstörungen, Myoklonus, Synkopen.

Selten: Krampfanfälle, Akathisie, buccoglossales Syndrom, Koma.

Sehr selten: Gedächtnisstörungen.

Serotonin-Syndrom wurde berichtet.

Augenerkrankungen

Häufig: Sehstörungen.

Gelegentlich: Mydriasis.

Herzerkrankungen

Häufig: Herzklopfen.

Gelegentlich: Angina Pectoris, Myokardinfarkt, Tachykardie (siehe «Überdosierung»).

Selten: Reizleitungs- bzw. Reizbildungsstörungen des Herzens.

Gefässerkrankungen

Häufig: Erröten.

Gelegentlich: Hypotonie.

Selten: Vasculitis, Vasodilatation, Thrombophlebitis.

Erkrankungen der Atemwege, des Brustraums und Mediastinums

Häufig: Gähnen.

Gelegentlich: Dyspnoe.

Selten: Pharyngitis.

Nasenbluten wurde berichtet.

Erkrankungen des Gastrointestinaltrakts

Sehr häufig: Diarrhö (11,0%), Übelkeit (18,5%).

Häufig: Erbrechen, Dyspepsie, Mundtrockenheit.

Gelegentlich: Dysphagie.

Selten: Schmerzen der Speiseröhre.

Sehr selten: Pankreatitis.

Gastrointestinale Blutungen, einschliesslich Ösophagusvarizenblutung, Blutungen von Zahnfleisch und Mund, Erbrechen von Blut, Blutstuhl, Hämatome (intraabdominal, peritoneal), Blutungen (anal, ösophageal, gastrisch, gastrointestinal (oberer und unterer Gastrointestinaltrakt), hämorrhoidal, peritoneal, rektal), hämorrhagische Diarrhö und Enterokolitis, hämorrhagische Divertikulitis, hämorrhagische Gastritis, Teerstuhl und hämorrhagisches Ulkus (ösophageal, gastrisch, duodenal), wurden gemeldet.

Leber- und Gallenerkrankungen

Häufig: abnorme Leberfunktionstests.

Sehr selten: Hepatitis.

Erkrankungen der Haut und des Unterhautzellgewebes

Häufig: Hautausschlag, Urtikaria, Pruritus, Hyperhidrose.

Gelegentlich: Alopezie, erhöhte Neigung zu Blutergüssen, kalter Schweiss. Exantheme, die sehr selten von systemischen Begleiterscheinungen wie Gelenksbeschwerden, Adenopathie und Fieber begleitet sein können.

Selten: Angioödem, Ekchymosen, Lichtempfindlichkeitsreaktion.

Erythema multiforme wurde berichtet, das zum Stevens-Johnson-Syndrom führen kann, oder toxische epidermale Nekrolyse (Lyell-Syndrom).

Skelettmuskulatur-, Bindegewebs- und Knochenerkrankungen

Gelegentlich: Muskelzuckungen.

Erkrankungen der Nieren und Harnwege

Häufig: häufiges Wasserlassen (einschliesslich Pollakisurie).

Gelegentlich: Dysurie.

Selten: Harnverhalten.

Blasenentleerungsstörungen wurden berichtet.

Erkrankungen der Geschlechtsorgane und der Brustdrüse

Häufig: gynäkologische Blutungen, erektile Dysfunktion, Ejakulationsstörungen.

Gelegentlich: sexuelle Funktionsstörungen (gelegentlich anhaltend nach Absetzen der Therapie), Galaktorrhö.

Selten: Hyperprolaktinämie (Amenorrhö, Brustvergrösserung etc.).

Priapismus wurde berichtet.

Allgemeine Erkrankungen und Beschwerden am Verabreichungsort

Sehr häufig: Müdigkeit (12,8%) (einschliesslich Asthenie).

Häufig: Nervositätsgefühl, Schüttelfrost.

Gelegentlich: Unwohlsein, Unbehagen, Hitzegefühl, Kältegefühl.

Systemische Symptome, die wahrscheinlich auf eine Vasculitis zurückzuführen sind, wurden sehr selten bei Patienten mit Hautausschlägen berichtet, in diesem Zusammenhang wurden Todesfälle gemeldet.

Ob diese systemischen Nebenwirkungen und die Hautausschläge eine gemeinsame zugrundeliegende Ursache haben, oder verschiedener Pathogenese sind, ist nicht bekannt. Immunbiologische Zusammenhänge konnten bisher nicht gefunden werden.

Überdosierung

Symptome

Fälle von Überdosierung von Fluoxetin allein haben gewöhnlich einen milden Verlauf. Symptome von Überdosierung: Übelkeit, Erbrechen, epileptische Anfälle, Herzfunktionsstörungen, welche von asymptomatischen Arrhythmien (einschliesslich AV-Knotenrhythmus und ventrikuläre Arrhythmien) oder EKG Veränderungen, die auf eine QTc-Zeit-Verlängerung hindeuten, bis zum kardialen Arrest (einschliesslich sehr seltener Fälle von Torsade de Pointes) reichen können, Lungenfunktionsstörungen und Anzeichen von verändertem ZNS- Zustand, welcher von Erregung bis Koma reichen kann. Tödlicher Ausgang, welcher mit Überdosierung von Fluoxetin allein in Zusammenhang gebracht wurde, war extrem selten.

Behandlung

Monitoring der kardialen und vitalen Parameter wird empfohlen, zusammen mit allgemeinen symptomatischen und unterstützenden Massnahmen. Es ist kein spezifisches Antidot bekannt. Forcierte Diurese, Dialyse, Hämoperfusion und Austauschtransfusion werden kaum von Nutzen sein wegen des grossen Verteilvolumens von Fluoxetin. Bei der Behandlung einer Überdosierung sollte die Möglichkeit, dass mehrere Arzneimittel eingenommen wurden, in Betracht gezogen werden.

Eigenschaften/Wirkungen

ATC-Code: N06AB03

Fluoxetin ist ein Antidepressivum zur oralen Anwendung, das chemisch weder mit tri- oder tetracyclischen noch anderen Antidepressiva verwandt ist. Aus Tierstudien wird angenommen, dass Fluoxetin, anders als tricyclische Antidepressiva, keinen direkten Einfluss auf noradrenerge oder dopaminerge Neuronen hat.

Die klinische Wirkung dürfte auf einer Hemmung der Wiederaufnahme des Serotonins in die präsynaptischen Neuronen beruhen. Bei Probanden, die eine Woche lang 30 mg Fluoxetin pro Tag erhalten haben, nahm die Serotonin-Aufnahme durch Blutplättchen um mehr als 60% ab.

Pharmakokinetik

Absorption

Fluoxetin wird nach oraler Verabreichung gut resorbiert (mindestens 85%). Plasmaspitzenspiegel treten 6 Stunden nach Verabreichung auf. Bei einmaliger oraler Verabreichung einer Dosis von 40 mg werden Plasmaspitzenspiegel in einem Bereich von 15 bis 55 ng/ml nach 6–8 Stunden beobachtet. Nach einer 30-tägigen Einnahme von 40 mg/Tag sind Plasmakonzentrationen von 91–302 ng/ml Fluoxetin und von 72–258 ng/ml Norfluoxetin beobachtet worden. Die Resorptionsgeschwindigkeit verlangsamt sich geringfügig bei gleichzeitiger Nahrungsaufnahme, das Ausmass der Resorption bleibt jedoch unverändert.

Metabolismus

Bei rund 3 bis 10% der gesunden Bevölkerung kommt es aufgrund eines genetischen Defektes zu einer Verringerung der Aktivität des Cytochrom-450-Isoenzyms 2D6. Solche Personen werden als «poor metabolizers» von Substanzen wie Debrisoquin, Dextromethorphan und trizyklischen Antidepressiva bezeichnet. Viele Substanzen, darunter auch die meisten Antidepressiva wie etwa Fluoxetin und andere selektive Serotoninaufnahmehemmer, werden durch dieses Isoenzym metabolisiert; deshalb sind die pharmakologischen Eigenschaften und relativen Anteile der Metaboliten bei «poor metabolizern» verändert. Jedoch ist im Falle von Fluoxetin und seinen Metaboliten die Summe der Plasmakonzentrationen der 4 aktiven Enantiomere zwischen «poor» und «fast metabolizern» vergleichbar.

Distribution

Das Verteilungsvolumen von Fluoxetin und des Desmethylmetaboliten von Fluoxetin (Norfluoxetin) beträgt 20 bis 45 Liter/kg Körpergewicht. Die Bindung an Serumprotein beträgt ca. 94,5%.

Elimination

Fluoxetin wird extensiv metabolisiert, sodass nur geringe Mengen unveränderter Muttersubstanz in den Harn ausgeschieden werden. Bei Untersuchungen mit radioaktiv markierter Substanz wurden nach 5 Wochen 60% der Radioaktivität im Harn und 16% in den Faeces wiederaufgefunden. Ein bekannter Metabolit ist das Desmethylfluoxetin Norfluoxetin, das ebenfalls die Aufnahme von Serotonin selektiv hemmt.

Bei gesunden Probanden beträgt die Halbwertszeit von Fluoxetin 4–6 Tage, die des Desmethylmetaboliten (Norfluoxetin) 4–16 Tage.

Die Plasmaclearance beträgt für Fluoxetin etwa 20 Liter/Std. und für Desmethylfluoxetin etwa 9 Liter/Std.

Bereich der optimalen Wirkkonzentration im Plasma

Ein Steady state der Plasmakonzentrationen wird nach 2–3 Wochen erreicht. Wirksame oder messbare Serumspiegel bleiben nach Absetzen des Arzneimittels noch während 5 Halbwertszeiten bestehen.

Die erreichten steady-state-Spiegel sind proportional der Dosierung, variieren aber von Patient zu Patient beträchtlich.

Kinetik spezieller Patientengruppen

Die pharmakokinetischen Profile von *älteren* Probanden wichen – bei Einmaldosierung – von jenen junger Probanden nicht signifikant ab.

Bei *Niereninsuffizienz* kommt es unter mehrfacher Verabreichung von Fluoxetin zu einer Kumulation, welche im Allgemeinen eine Dosisanpassung erfordert.

Bei Patienten mit fortgeschrittener *Leberzirrhose* ist die Elimination von Fluoxetin deutlich vermindert. Die Halbwertszeit von Fluoxetin verlängert sich im Durchschnitt auf 7,6 (üblicherweise 4–6 Tage), die von Norfluoxetin auf 12 Tage (üblicherweise 4–16 Tage).

In all diesen 3 Situationen wird eine Dosisanpassung empfohlen (siehe «Dosierung/Anwendung»).

Bis jetzt liegen keine Daten am Menschen über die Verteilung von Fluoxetin in Liquor oder über den plazentaren Übergang vor.

Präklinische Daten

Es gibt keine Hinweise auf Karzinogenität oder Mutagenität aus *In-vitro*- oder Tierstudien. Bei adulten Tieren wurde keine Beeinträchtigung der Fertilität bei Dosierungen bis zu 12,5 mg/kg/Tag (ungefähr das 1,5fache der maximal beim Menschen empfohlene Dosis in mg/m²) beobachtet.

Reproduktionstoxikologie

Embryofetale Entwicklungsstudien an Ratten und Kaninchen haben nach Verabreichung von bis zu 12,5 bzw. 15 mg/kg/Tag (des 1,5- bzw. 3,6fachen der maximal empfohlenen Dosis beim Menschen [MRHD] von 80 mg auf mg/m² Basis) während der gesamten Organogenese keine Befunde für eine Teratogenität ergeben. In Reproduktionsstudien an Ratten kam es jedoch zu einer Zunahme der Anzahl der totgeborenen Jungen, einer Abnahme des Gewichts der Jungen und einer Erhöhung der Sterblichkeit der Jungen während der ersten 7 Tage postpartum, wenn die Muttertiere während der Gestation 12 mg/kg/Tag (das 1,5fache der MRHD auf mg/m²-Basis) oder 7,5 mg/kg/Tag (das 0,9fache der MRHD auf mg/m²-Basis) während der Gestation und Laktation erhielten. Bei den überlebenden Nachkommen von Ratten, die während der Gestation mit 12 mg/kg/Tag behandelt wurden, ergaben sich keine Befunde für eine Entwicklungsneurotoxizität. Die No-Effect-Dosis für die postpartale Rattenmortalität betrug 5 mg/kg/Tag (das 0,6fache der MRHD auf mg/m²-Basis).

Sonstige Hinweise

Haltbarkeit

Das Arzneimittel darf nur bis zu dem auf dem Behälter mit «Exp.» bezeichneten Datum verwendet werden.

Besondere Lagerungshinweise

Das Arzneimittel in der Originalpackung, bei Raumtemperatur (15–25 °C) und ausser Reichweite von Kindern aufbewahren.

Zulassungsnummer

54492, 57175 (Swissmedic).

Packungen

Fluoxetin Sandoz Kaps 14. (B)

Fluoxetin Sandoz Kaps 30. (B)

Fluoxetin Sandoz Kaps 100. (B)

Fluoxetin Sandoz Tabl 14 (dispergierbar, teilbar). (B)

Fluoxetin Sandoz Tabl 28 (dispergierbar, teilbar). (B)

Fluoxetin Sandoz Tabl 100 (dispergierbar, teilbar). (B)

Zulassungsinhaberin

Sandoz Pharmaceuticals AG, Risch.

Domizil

Rotkreuz.

Stand der Information

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National Institute for Health and Clinical Excellence

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Depression in children and young people

Identification and management in primary, community and secondary care

Clinical Guideline 28

Developed by the National Collaborating Centre for Mental Health

Clinical Guideline 28
Depression in children and young people: identification and management in primary, community and secondary care

Ordering information
You can download the following documents from www.nice.org.uk/CG028

- The NICE guideline (this document) – all the recommendations.
- A quick reference guide, which has been distributed to healthcare professionals working in the NHS in England.
- Information for children and young people with depression, their families and carers, and the public.
- The full guideline – all the recommendations, details of how they were developed, and summaries of the evidence on which they were based.

For printed copies of the quick reference guide or information for the public, phone the NHS Response Line on 0870 1555 455 and quote:

- N0910 (quick reference guide)
- N0911 (information for the public).

This guidance is written in the following context

This guidance represents the view of the Institute, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. The guidance does not, however, override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

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Contents

Patient-centred care

This guideline offers best practice advice on the care of children and young people with depression.

Treatment and care should take into account the child's or young person's individual needs and preferences as well as the wishes of the parent(s) or carer(s).

Children and young people with depression should have the opportunity to make informed decisions about their care and treatment, but this does depend on their age and capacity to make decisions. It is good practice for healthcare professionals to involve the young person's parent(s) or carer(s) in the decision-making process. Where a child or young person is not old enough or does not have the capacity to make decisions, healthcare professionals should follow the Department of Health guidelines – *Reference guide to consent for examination or treatment* (2001) (available from www.dh.gov.uk).

Good communication between healthcare professionals and children or young people and their parent(s) or carer(s) is essential. It should be supported by the provision of evidence-based information offered in a form that is tailored to the needs of the individual. The treatment, care and information provided should be culturally appropriate and in a form that is accessible to people who have additional needs, such as people with physical, cognitive or sensory disabilities, and people who do not speak or read English.

Unless specifically excluded by the child or young person, parent(s) or carer(s) should have the opportunity to be involved in decisions about the child or young person's care and treatment.

The parent(s) and carer(s) should also be provided with the information and support they need.

Key priorities for implementation

The following recommendations have been identified as priorities for implementation.

Assessment and coordination of care

- When assessing a child or young person with depression, healthcare professionals[1] should routinely consider, and record in the patient's notes, potential comorbidities, and the social, educational and family context for the patient and family members, including the quality of interpersonal relationships, both between the patient and other family members and with their friends and peers.

Treatment considerations in all settings

- Psychological therapies used in the treatment of children and young people should be provided by therapists who are also trained child and adolescent mental healthcare professionals.
- Comorbid diagnoses and developmental, social and educational problems should be assessed and managed, either in sequence or in parallel, with the treatment for depression. Where appropriate this should be done through consultation and alliance with a wider network of education and social care.
- Attention should be paid to the possible need for parents' own psychiatric problems (particularly depression) to be treated in parallel, if the child or young person's mental health is to improve. If such a need is identified, then a plan for obtaining such treatment should be made, bearing in mind the availability of adult mental health provision and other services.

Step 1: Detection and risk profiling

- Healthcare professionals in primary care, schools and other relevant community settings should be trained to detect symptoms of depression, and to assess children and young people who may be at risk of

[1] See page 63 for the glossary definition of healthcare professionals as used in this guideline.

depression. Training should include the evaluation of recent and past psychosocial risk factors, such as age, gender, family discord, bullying, physical, sexual or emotional abuse, comorbid disorders, including drug and alcohol use, and a history of parental depression; the natural history of single loss events; the importance of multiple risk factors; ethnic and cultural factors; and factors known to be associated with a high risk of depression and other health problems, such as homelessness, refugee status and living in institutional settings.

- Child and Adolescent Mental Health Services (CAMHS) tier 2 or 3 should work with health and social care professionals in primary care, schools and other relevant community settings to provide training and develop ethnically and culturally sensitive systems for detecting, assessing, supporting and referring children and young people who are either depressed or at significant risk of becoming depressed.

Step 2: Recognition

- Training opportunities should be made available to improve the accuracy of CAMHS professionals in diagnosing depressive conditions. The existing interviewer-based instruments (such as Kiddie-Sads [K-SADS] and Child and Adolescent Psychiatric Assessment [CAPA]) could be used for this purpose but will require modification for regular use in busy routine CAMHS settings.

Step 3: Mild depression

- Antidepressant medication should not be used for the initial treatment of children and young people with mild depression.

Steps 4 and 5: Moderate to severe depression

- Children and young people with moderate to severe depression should be offered, as a first-line treatment, a specific psychological therapy (individual cognitive behavioural therapy [CBT], interpersonal therapy or shorter-term family therapy; it is suggested that this should be of at least 3 months' duration).

- Antidepressant medication should not be offered to a child or young person with moderate to severe depression except in combination with a concurrent psychological therapy. Specific arrangements must be made for careful monitoring of adverse drug reactions, as well as for reviewing mental state and general progress; for example, weekly contact with the child or young person and their parent(s) or carer(s) for the first 4 weeks of treatment. The precise frequency will need to be decided on an individual basis, and recorded in the notes. In the event that psychological therapies are declined, medication may still be given, but as the young person will not be reviewed at psychological therapy sessions, the prescribing doctor should closely monitor the child or young person's progress on a regular basis and focus particularly on emergent adverse drug reactions.

The following guidance is evidence based. The grading scheme used for the recommendations (A, B, C or good practice point [GPP]) is described in Appendix A; a summary of the evidence on which the guidance is based is provided in the full guideline (see Section 5.1).

1 Guidance

This guideline makes recommendations for the identification and treatment of depression in children (5–11 years) and young people (from the age of 12 up to their 18th birthday) in primary, community and secondary care. Depression is a broad and heterogeneous diagnostic grouping, central to which is depressed mood or loss of pleasure in most activities. Depressive symptoms are frequently accompanied by symptoms of anxiety, but may also occur on their own. *The ICD-10 Classification of Mental and Behavioural Disorders* (World Health Organization, 1992) uses an agreed list of 10 depressive symptoms, and divides the common form of major depressive episode into four groups: not depressed (fewer than four symptoms), mild depression (four symptoms), moderate depression (five to six symptoms), and severe depression (seven or more symptoms, with or without psychotic symptoms). Symptoms should be present for at least 2 weeks and every symptom should be present for most of the day.

For the purposes of this guideline, the treatment and management of depression have been divided into the following descriptions as defined by ICD-10:

- mild depression
- moderate and severe depression
- severe depression with psychotic symptoms.

However, it is doubtful whether the severity of the depressive illness can realistically be captured in a single symptom count. Clinicians will wish to consider family context and previous history, as well as the degree of associated impairment, in making this assessment (see Appendix E). Thus it is important not just to enquire about specific symptoms but to explore the

child or young person's functioning (and impairment of functioning) in a number of settings, for example, at school, with peers and with family. Children and young people with a chronic subclinical version of depression that has persisted for over a year – known as dysthymia – should be treated as for mild depression. The guideline also makes recommendations about the management of children and young people with recurrent depression.

The guideline draws on the best currently available evidence for the identification and management of depression. However, there are some significant limitations to the current evidence base, which have considerable implications for this guideline. These include the relatively small number of published studies of psychological therapies; concern about unpublished studies of pharmacological treatment; small, non-clinical, and sometimes unrepresentative samples with wide age ranges in the published pharmacological studies; a lack of consistency in reporting adverse drug reactions; a dearth of studies comparing efficacy and adverse reactions to psychological with pharmacological treatments (with one recent exception); and very limited data on long-term outcomes.

However, the most significant limitation is the concept of depression itself. The view of the Guideline Development Group is that it is too broad and heterogeneous a category, and has limited validity as a basis for effective treatment plans. A focus on symptoms alone is not sufficient because a wide range of biological, psychological and social factors have a significant impact on response to treatment and are not captured by the current diagnostic systems.

The guideline makes evidence-based recommendations and good practice points for the psychological, pharmacological, physical and self-help interventions appropriate to the severity of the depression. In addition, the first part of the guideline makes good practice points and recommendations relevant to the care of all children and young people with depression.

Prescribing antidepressants for children and young people

At the date of publication (September 2005), there are no antidepressant drugs with a current UK Marketing Authorisation for depression in children and young people (under 18 years).[2] However, in 2000, the Royal College of Paediatrics and Child Health issued a policy statement on the use of unlicensed medicines, or the use of licensed medicines for unlicensed applications, in children and young people. This states that such use is necessary in paediatric practice and that doctors are legally allowed to prescribe unlicensed medicines where there are no suitable alternatives and where the use is justified by a responsible body of professional opinion.[3]

In December 2003, following a review by an Expert Working Group of the Committee on Safety of Medicines (CSM), the CSM advised that, despite the lack of a marketing authorisation for fluoxetine in the treatment of major depressive disorder in under 18s at that time, the balance of risks and benefits for this drug was favourable. The CSM also stated that sertraline, citalopram and escitalopram, paroxetine, venlafaxine and fluvoxamine should not be used as new therapy.[4] However, its advice was clear that child and adolescent psychiatrists are able to prescribe selective serotonin reuptake inhibitors (SSRIs) other than fluoxetine in certain circumstances; for example, where drug treatment is indicated but a patient is intolerant of fluoxetine.

In April 2005 the Committee on Human Medicinal Products (CHMP) of the European Medicines Evaluation Agency (EMEA) also issued advice on the paediatric use of SSRIs and serotonin noradrenaline reuptake inhibitors (SNRIs). This advice referred to all uses of these drugs in paediatrics, not just the treatment of depression. The CHMP advised that these products should not be used in children and adolescents except within their approved indications – not usually depression – because of the risk of suicide-related

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[2] Check the Summary of Product Characteristics of individual drugs for current licensed indications.
[3] Joint Royal College of Paediatrics and Child Health/Neonatal and Paediatric Pharmacists Group Standing Committee on Medicines (2000) *The Use of Unlicensed Medicines or Licensed Medicines for Unlicensed Applications in Paediatric Practice - Policy Statement*. London: Royal College of Paediatrics and Child Health.
[4] The CSM advice can be found at http://medicines.mhra.gov.uk/aboutagency/regframework/csm/csmhome.htm

behaviour and hostility. However, like the CSM, the CHMP also made it clear that doctors may make decisions based on the individual clinical needs of a child or an adolescent to use these products for the treatment of depression or anxiety. In such circumstances the CHMP recommended that patients be monitored carefully for the appearance of suicidal behaviour, self-harm or hostility, particularly at the beginning of treatment.

1.1 Care of all children and young people with depression

1.1.1 Good information, informed consent and support

Children and young people and their families need good information, given as part of a collaborative and supportive relationship with healthcare professionals, and need to be able to give fully informed consent.

1.1.1.1 Healthcare professionals involved in the detection, assessment or treatment of children or young people with depression should ensure that information is provided to the patient and their parent(s) and carer(s) at an appropriate time. The information should be age appropriate and should cover the nature, course and treatment of depression, including the likely side-effect profile of medication should this be offered. **GPP**

1.1.1.2 Healthcare professionals involved in the treatment of children or young people with depression should take time to build a supportive and collaborative relationship with both the patient and the family or carers. **GPP**

1.1.1.3 Healthcare professionals should make all efforts necessary to engage the child or young person and their parent(s) or carer(s) in treatment decisions, taking full account of patient and parental/carer expectations, so that the patient and their parent(s) or carer(s) can give meaningful and properly informed consent before treatment is initiated. **GPP**

1.1.1.4 Families and carers should be informed of self-help groups and support groups and be encouraged to participate in such programmes where appropriate. **GPP**

1.1.2 Language and ethnic minorities

Information should be provided in a language and format that a child or young person and their family or carer(s) can properly understand; interpreters should be engaged when needed. Psychological treatments are also best conducted in the child or young person's first language. Healthcare professionals should be trained to understand the specific needs of depressed children or young people from black and minority ethnic groups. Patients, families and carers, including those from black and minority ethnic groups, should be involved in planning services.

1.1.2.1 Where possible, all services should provide written information or audiotaped material in the language of the child or young person and their family or carer(s), and professional interpreters should be sought for those whose preferred language is not English. **GPP**

1.1.2.2 Consideration should be given to providing psychological therapies and information about medication and local services in the language of the child or young person and their family or carers where the patient's and/or their family's or carer's first language is not English. If this is not possible, an interpreter should be sought. **GPP**

1.1.2.3 Healthcare professionals in primary, secondary and relevant community settings should be trained in cultural competence to aid in the diagnosis and treatment of depression in children and young people from black and minority ethnic groups. This training should take into consideration the impact of the patient's and healthcare professional's racial identity status on the patient's depression. **GPP**

1.1.2.4 Healthcare professionals working with interpreters should be provided with joint training opportunities with those interpreters, to ensure that both healthcare professionals and interpreters understand

the specific requirements of interpretation in a mental health setting. **GPP**

1.1.2.5 The development and evaluation of services for children and young people with depression should be undertaken in collaboration with stakeholders involving patients and their families and carers, including members of black and minority ethnic groups. **GPP**

1.1.3 Assessment and coordination of care

The assessment of children and young people should be comprehensive and holistic, taking into account drug and alcohol use, the risks of self-harm and suicidal ideations, and the use of self-help materials and methods. Parental depression may be an important contributing factor and needs to be identified.

1.1.3.1 When assessing a child or young person with depression, healthcare professionals should routinely consider, and record in the patient's notes, potential comorbidities, and the social, educational and family context for the patient and family members, including the quality of interpersonal relationships, both between the patient and other family members and with their friends and peers. **GPP**

1.1.3.2 In the assessment of a child or young person with depression, healthcare professionals should always ask the patient and their parent(s) or carer(s) directly about the child or young person's alcohol and drug use, any experience of being bullied or abused, self-harm and ideas about suicide. A young person should be offered the opportunity to discuss these issues initially in private. **GPP**

1.1.3.3 If a child or young person with depression presents acutely having self-harmed, the immediate management should follow the NICE guideline 'Self-harm: the short-term physical and psychological management and secondary prevention of self-harm in primary and secondary care' (www.nice.org.uk/CG016) as this applies to children and young people, paying particular attention to the guidance on

consent and capacity. Further management should then follow this depression guideline. **GPP**

1.1.3.4 In the assessment of a child or young person with depression, healthcare professionals should always ask the patient, and be prepared to give advice, about self-help materials or other methods used or considered potentially helpful by the patient or their parent(s) or carer(s). This may include educational leaflets, helplines, self-diagnosis tools, peer, social and family support groups, complementary therapies, and religious and spiritual groups. **GPP**

1.1.3.5 Healthcare professionals should only recommend self-help materials or strategies as part of a supported and planned package of care. **GPP**

1.1.3.6 For any child or young person with suspected mood disorder, a family history should be obtained to check for unipolar or bipolar depression in parents and grandparents. **GPP**

1.1.3.7 When a child or young person has been diagnosed with depression, consideration should be given to the possibility of parental depression, parental substance misuse, or other mental health problems and associated problems of living, as these are often associated with depression in a child or young person and, if untreated, may have a negative impact on the success of treatment offered to the child or young person. **GPP**

1.1.3.8 When the clinical progress of children and young people with depression is being monitored in secondary care, the self-report Mood and Feelings Questionnaire (MFQ) should be considered as an adjunct to clinical judgement. **C**

1.1.3.9 In the assessment and treatment of depression in children and young people, special attention should be paid to the issues of: **GPP**

- confidentiality
- the young person's consent (including Gillick competence)
- parental consent
- child protection
- the use of the Mental Health Act in young people
- the use of the Children Act.

1.1.3.10 The form of assessment should take account of cultural and ethnic variations in communication, family values and the place of the child or young person within the family. **GPP**

1.1.4 The organisation and planning of services

Better links between Child and Adolescent Mental Health Services (CAMHS) and tier 1 and tier 2 are needed to improve detection and availability of treatment (see glossary for explanations of tiers). All healthcare professionals should monitor detection rates and record outcomes for local planning and local, regional and national comparison.

1.1.4.1 Healthcare professionals specialising in depression in children and young people should work with local CAMHS to enhance specialist knowledge and skills regarding depression in these existing services. This work should include providing training and help with guideline implementation. **GPP**

1.1.4.2 CAMHS and primary care trusts (PCTs) should consider introducing a primary mental health worker (or CAMHS link worker) (see glossary) into each secondary school and secondary pupil referral unit as part of tier 2 provision within the locality. **GPP**

1.1.4.3 Primary mental health workers (or CAMHS link workers) should establish clear lines of communication between CAMHS and tier 1 or 2, with named contact people in each tier or service, and develop

systems for the collaborative planning of services for young people with depression in tiers 1 and 2. **GPP**

1.1.4.4 CAMHS and PCTs should routinely monitor the rates of detection, referral and treatment of children and young people, from all ethnic groups, with mental health problems, including those with depression, in local schools and primary care. This information should be used for planning services and made available for local, regional and national comparison. **GPP**

1.1.4.5 All healthcare professionals should routinely use, and record in the notes, appropriate outcome measures (such as those self-report measures used in screening for depression or generic outcome measures used by particular services, for example Health of the Nation Outcome Scale for Children and Adolescents [HoNOSCA] or Strengths and Difficulties Questionnaire [SDQ]), for the assessment and treatment of depression in children and young people. This information should be used for planning services, and made available for local, regional and national comparison. **GPP**

1.1.5 Treatment considerations in all settings

Most treatment should be undertaken in outpatient settings or the community. Before treatment is started the social networks around the child or young person need to be clearly identified. If bullying is a factor, school and healthcare professionals should jointly develop antibullying strategies. Psychological treatments should be provided by professionally trained therapists, who should aim to quickly develop an alliance with the child or young person and their family or carer(s). Comorbid conditions will also need to be treated and interventions considered for parents with depression or other significant personal problems. Advice about exercise, sleep and nutrition should also be considered.

1.1.5.1 Most children and young people with depression should be treated on an outpatient or community basis. **C**

1.1.5.2 Before any treatment is started, healthcare professionals should assess, together with the young person, the social network around him or her. This should include a written formulation, identifying factors that may have contributed to the development and maintenance of depression, and that may impact both positively or negatively on the efficacy of the treatments offered. The formulation should also indicate ways that the healthcare professionals may work in partnership with the social and professional network of the young person. **B**

1.1.5.3 When bullying is considered to be a factor in a child or young person's depression, CAMHS, primary care and educational professionals should work collaboratively to prevent bullying and to develop effective antibullying strategies. **C**

1.1.5.4 Psychological therapies used in the treatment of children and young people with depression should be provided by therapists who are also trained child and adolescent mental healthcare professionals. **B**

1.1.5.5 Psychological therapies used in the treatment of children and young people with depression should be provided by healthcare professionals who have been trained to an appropriate level of competence in the specific modality of psychological therapy being offered. **C**

1.1.5.6 Therapists should develop a treatment alliance with the family. If this proves difficult, consideration should be given to providing the family with an alternative therapist. **C**

1.1.5.7 Comorbid diagnoses and developmental, social and educational problems should be assessed and managed, either in sequence or in parallel, with the treatment for depression. Where appropriate this should be done through consultation and alliance with a wider network of education and social care. **B**

1.1.5.8 Attention should be paid to the possible need for parents' own psychiatric problems (particularly depression) to be treated in parallel, if the child or young person's mental health is to improve. If such a need is identified, then a plan for obtaining such treatment should be made, bearing in mind the availability of adult mental health provision and other services. **B**

1.1.5.9 A child or young person with depression should be offered advice on the benefits of regular exercise and encouraged to consider following a structured and supervised exercise programme of typically up to three sessions per week of moderate duration (45 minutes to 1 hour) for between 10 and 12 weeks. **C**

1.1.5.10 A child or young person with depression should be offered advice about sleep hygiene and anxiety management. **C**

1.1.5.11 A child or young person with depression should be offered advice about nutrition and the benefits of a balanced diet. **GPP**

1.2 Stepped care

The stepped-care model of depression draws attention to the different needs that depressed children and young people have – depending on the characteristics of their depression and their personal and social circumstances – and the responses that are required from services. It provides a framework in which to organise the provision of services that support both healthcare professionals and patients and their parent(s) or carer(s) in identifying and accessing the most effective interventions (see Table 1).

Table 1 The stepped-care model.

Focus	Action	Responsibility
Detection	Risk profiling	Tier 1
Recognition	Identification in presenting children or young people	Tiers 2–4
Mild depression (including dysthymia)	Watchful waiting Non-directive supportive therapy/group cognitive behavioural therapy/guided self-help	Tier 1 Tier 1 or 2
Moderate to severe depression	Brief psychological therapy +/– fluoxetine	Tier 2 or 3
Depression unresponsive to treatment/recurrent depression/psychotic depression	Intensive psychological therapy +/– fluoxetine, sertraline, citalopram, augmentation with an antipsychotic	Tier 3 or 4

The guidance follows these five steps.

1. Detection and recognition of depression and risk profiling in primary care and community settings.
2. Recognition of depression in children and young people referred to CAMHS.
3. Managing recognised depression in primary care and community settings – mild depression.
4. Managing recognised depression in tier 2 or 3 CAMHS – moderate to severe depression.
5. Managing recognised depression in tier 3 or 4 CAMHS – unresponsive, recurrent and psychotic depression, including depression needing inpatient care.

Each step introduces additional interventions; the higher steps assume interventions in the previous step.

1.3 Step 1: Detection, risk profiling and referral

Healthcare professionals working with children or young people in primary care, schools and the community need training to assess the risk of depression, to provide emotional support and know when to refer, especially when a child or young person has experienced an undesirable life event. CAMHS tier 2 or 3 should work with tier 1 healthcare professionals and help provide training in the recognition of depression.

1.3.1 Detection and risk profiling

1.3.1.1 Healthcare professionals in primary care, schools and other relevant community settings should be trained to detect symptoms of depression, and to assess children and young people who may be at risk of depression. Training should include the evaluation of recent and past psychosocial risk factors, such as age, gender, family discord, bullying, physical, sexual or emotional abuse, comorbid disorders, including drug and alcohol use, and a history of parental depression; the natural history of single loss events; the importance of multiple risk factors; ethnic and cultural factors; and factors known to be associated with a high risk of depression and other health problems, such as homelessness, refugee status and living in institutional settings. **C**

1.3.1.2 Healthcare professionals in primary care, schools and other relevant community settings should be trained in communications skills such as ‘active listening’ and ‘conversational technique’, so that they can deal confidently with the acute sadness and distress (‘situational dysphoria’) that may be encountered in children and young people following recent undesirable events. **GPP**

1.3.1.3 Healthcare professionals in primary care settings should be familiar with screening for mood disorders. They should have regular access to specialist supervision and consultation. **GPP**

1.3.1.4 Healthcare professionals in primary care, schools and other relevant community settings who are providing support for a child or young person with situational dysphoria should consider ongoing social and environmental factors if the dysphoria becomes more persistent. **GPP**

1.3.1.5 Child and Adolescent Mental Health Services (CAMHS) tier 2 or 3 should work with health and social care professionals in primary care, schools and other relevant community settings to provide training and develop ethnically and culturally sensitive systems for detecting, assessing, supporting and referring children and young people who are either depressed or at significant risk of becoming depressed. **GPP**

1.3.1.6 In the provision of training by CAMHS professionals for healthcare professionals in primary care, schools and relevant community settings, priority should be given to the training of pastoral support staff in schools (particularly secondary schools), community paediatricians and GPs. **GPP**

1.3.1.7 When a child or young person is exposed to a single recent undesirable life event, such as bereavement, parental divorce or separation or a severely disappointing experience, healthcare professionals in primary care, schools and other relevant community settings should undertake an assessment of the risks of depression associated with the event and make contact with their parent(s) or carer(s) to help integrate parental/carer and professional responses. The risk profile should be recorded in the child or young person's records. **C**

1.3.1.8 When a child or young person is exposed to a single recent undesirable life event, such as bereavement, parental divorce or separation or a severely disappointing experience, in the absence of other risk factors for depression, healthcare professionals in primary care, schools and other relevant community settings should offer

support and the opportunity to talk over the event with the child or young person. **GPP**

1.3.1.9 Following an undesirable event, a child or young person should not normally be referred for further assessment or treatment, as single events are unlikely to lead to a depressive illness. **C**

1.3.1.10 A child or young person who has been exposed to a recent undesirable life event, such as bereavement, parental divorce or separation or a severely disappointing experience and is identified to be at high risk of depression (the presence of two or more other risk factors for depression), should be offered the opportunity to talk over their recent negative experiences with a professional in tier 1 and assessed for depression. Early referral should be considered if there is evidence of depression and/or self-harm. **GPP**

1.3.1.11 When a child or young person is exposed to a recent undesirable life event, such as bereavement, parental divorce or separation or a severely disappointing experience, and where one or more family members (parents or children) have multiple-risk histories for depression, they should be offered the opportunity to talk over their recent negative experiences with a professional in tier 1 and assessed for depression. Early referral should be considered if there is evidence of depression and/or self-harm. **GPP**

1.3.1.12 If children and young people who have previously recovered from moderate or severe depression begin to show signs of a recurrence of depression, healthcare professionals in primary care, schools or other relevant community settings should refer them to CAMHS tier 2 or 3 for rapid assessment. **GPP**

1.3.2 Referral criteria

1.3.2.1 For children and young people, the following factors should be used by healthcare professionals as indications that management can remain at tier 1: **GPP**

- exposure to a single undesirable event in the absence of other risk factors for depression
- exposure to a recent undesirable life event in the presence of two or more other risk factors with **no** evidence of depression and/or self-harm
- exposure to a recent undesirable life event, where one or more family members (parents or children) have multiple-risk histories for depression, providing that there is **no** evidence of depression and/or self-harm in the child or young person
- mild depression without comorbidity.

1.3.2.2 For children and young people, the following factors should be used by healthcare professionals as criteria for referral to tier 2 or 3 CAMHS: **GPP**

- depression with two or more other risk factors for depression
- depression where one or more family members (parents or children) have multiple-risk histories for depression
- mild depression in those who have not responded to interventions in tier 1 after 2–3 months
- moderate or severe depression (including psychotic depression)
- signs of a recurrence of depression in those who have recovered from previous moderate or severe depression
- unexplained self-neglect of at least 1 month's duration that could be harmful to their physical health
- active suicidal ideas or plans
- referral requested by a young person or their parent(s) or carer(s).

1.3.2.3 For children and young people, the following factors should be used by healthcare professionals as criteria for referral to tier 4 services: **GPP**

- high recurrent risk of acts of self-harm or suicide
- significant ongoing self-neglect (such as poor personal hygiene or significant reduction in eating that could be harmful to their physical health)

- requirement for intensity of assessment/treatment and/or level of supervision that is not available in tier 2 or 3.

1.4 Step 2: Recognition

CAMHS professionals need to improve their ability to recognise depression.

1.4.1 Children and young people of 11 years or older referred to CAMHS without a diagnosis of depression should be routinely screened with a self-report questionnaire for depression (of which the Mood and Feelings Questionnaire [MFQ] is currently the best) as part of a general assessment procedure. **B**

1.4.2 Training opportunities should be made available to improve the accuracy of CAMHS professionals in diagnosing depressive conditions. The existing interviewer-based instruments (such as Kiddie-Sads [K-SADS] and Child and Adolescent Psychiatric Assessment [CAPA]) could be used for this purpose but will require modification for regular use in busy routine CAMHS settings. **C**

1.4.3 Within tier 3 CAMHS, professionals who specialise in the treatment of depression should have been trained in interviewer-based assessment instruments (such as K-SADS and CAPA) and have skills in non-verbal assessments of mood in younger children. **GPP**

1.5 Step 3: Mild depression

Some children and young people diagnosed with mild depression may not need or want a specific intervention, but they need to be monitored and followed up, especially if they miss appointments.

1.5.1 Watchful waiting

1.5.1.1 For children and young people with diagnosed mild depression who do not want an intervention or who, in the opinion of the healthcare

professional, may recover with no intervention, a further assessment should be arranged, normally within 2 weeks ('watchful waiting'). **C**

1.5.1.2 Healthcare professionals should make contact with children and young people with depression who do not attend follow-up appointments. **C**

1.5.2 Interventions for mild depression

After up to 4 weeks of watchful waiting, children and young people with continuing mild depression should be offered a course of non-directive supportive therapy, group cognitive behavioural therapy (CBT) or guided self-help. Ideally this should be offered by appropriately trained professionals in tier 1 (primary care, schools, social services and the voluntary sector) but may require a referral to tier 2 CAMHS depending on local resources. If this is ineffective within 2 to 3 months, they should be referred for assessment by a tier 2 or 3 CAMHS team. Antidepressant medication should not be used in the initial treatment of mild depression.

1.5.2.1 Following a period of up to 4 weeks of watchful waiting, all children and young people with continuing mild depression and without significant comorbid problems or signs of suicidal ideation should be offered individual non-directive supportive therapy, group CBT or guided self-help for a limited period (approximately 2 to 3 months). This could be provided by appropriately trained professionals in primary care, schools, social services and the voluntary sector or in tier 2 CAMHS. **B**

1.5.2.2 Children and young people with mild depression who do not respond after 2 to 3 months to non-directive supportive therapy, group CBT or guided self-help should be referred for review by a tier 2 or 3 CAMHS team. **GPP**

1.5.2.3 Antidepressant medication should not be used for the initial treatment of children and young people with mild depression. **B**

1.5.2.4 The further treatment of children and young people with persisting mild depression unresponsive to treatment at tier 1 or 2 should follow the guidance for moderate to severe depression (see Section 1.6 below). **GPP**

1.6 Steps 4 and 5: Moderate to severe depression

There is little research evidence on the effectiveness of treatments for the younger child (5–11 years) with moderate to severe depression. In particular, there is little evidence for the effectiveness of antidepressant medication in children, which should, therefore, only be used very cautiously in this age group. In other respects, the recommended treatments for children are based upon the evidence for effectiveness in young people (12–18 years).

In children and young people psychological therapies are the first-line treatments.

1.6.1 Treatments for moderate to severe depression

All children and young people with moderate to severe depression should be assessed by CAMHS tier 2 or 3 professionals and offered a specific psychological therapy as a first-line treatment.

1.6.1.1 Children and young people presenting with moderate to severe depression should be reviewed by a CAMHS tier 2 or 3 team. **B**

1.6.1.2 Children and young people with moderate to severe depression should be offered, as a first-line treatment, a specific psychological therapy (individual cognitive behavioural therapy [CBT], interpersonal therapy or shorter-term family therapy); it is suggested that this should be of at least 3 months' duration. **B**

1.6.2 Combined treatments for moderate to severe depression

If there is no response to a specific psychological therapy within four to six sessions, then review and consider alternative or additional psychological

therapies for coexisting problems. Consider combining psychological therapy with fluoxetine[5] (cautiously in younger children). If combined treatment is not effective within a further six sessions, review and consider more intensive psychological therapy.

1.6.2.1 If moderate to severe depression in a child or young person is unresponsive to psychological therapy after four to six treatment sessions, a multidisciplinary review should be carried out. **GPP**

1.6.2.2 Following multidisciplinary review, if the child or young person's depression is not responding to psychological therapy as a result of other coexisting factors such as the presence of comorbid conditions, persisting psychosocial risk factors such as family discord, or the presence of parental mental ill-health, alternative or perhaps additional psychological therapy for the parent or other family members, or alternative psychological therapy for the patient, should be considered. **C**

1.6.2.3 Following multidisciplinary review, if moderate to severe depression in a **young person** (12–18 years) is unresponsive to a specific psychological therapy after four to six sessions, fluoxetine should be offered. **B**

1.6.2.4 Following multidisciplinary review, if moderate to severe depression in a **child** (5–11 years) is unresponsive to a specific psychological therapy after four to six sessions, the addition of fluoxetine should be **cautiously** considered, although the evidence for its effectiveness in this age group is not established. **C**

1.6.3 Depression unresponsive to combined treatment

1.6.3.1 If moderate to severe depression in a child or young person is unresponsive to combined treatment with a specific psychological

[5] Fluoxetine does not have a UK Marketing Authorisation for use in children and adolescents under the age of 18 at the date of publication (September 2005); check the Summary of Product Characteristics for current licensed indications; see also page 10.

therapy and fluoxetine after a further six sessions, or the patient and/or their parent(s) or carer(s) have declined the offer of fluoxetine, the multidisciplinary team should make a full needs and risk assessment. This should include a review of the diagnosis, examination of the possibility of comorbid diagnoses, reassessment of the possible individual, family and social causes of depression, consideration of whether there has been a fair trial of treatment, and assessment for further psychological therapy for the patient and/or additional help for the family. **GPP**

1.6.3.2 Following multidisciplinary review, the following should be considered: **B**

- an alternative psychological therapy which has not been tried previously (individual CBT, interpersonal therapy or shorter-term family therapy, of at least 3 months' duration), or
- systemic family therapy (at least 15 fortnightly sessions), or
- individual child psychotherapy (approximately 30 weekly sessions).

1.6.4 How to use antidepressants in children and young people

All antidepressant drugs have significant risks when given to children and young people with depression and, with the exception of fluoxetine, there is little evidence that they are effective in this context. Although fluoxetine can cause significant adverse drug reactions, it is safer when combined with psychological therapies. The following guidance outlines how fluoxetine should be used, and suggests possible alternatives in the event that fluoxetine is ineffective or not tolerated because of side effects.

1.6.4.1 Antidepressant medication should not be offered to a child or young person with moderate to severe depression except in combination with a concurrent psychological therapy. Specific arrangements must be made for careful monitoring of adverse drug reactions, as well as for reviewing mental state and general progress; for example, weekly contact with the child or young person and their parent(s) or carer(s)

for the first 4 weeks of treatment. The precise frequency will need to be decided on an individual basis, and recorded in the notes. In the event that psychological therapies are declined, medication may still be given, but as the young person will not be reviewed at psychological therapy sessions, the prescribing doctor should closely monitor the child or young person's progress on a regular basis and focus particularly on emergent adverse drug reactions. **B**

1.6.4.2 If an antidepressant is to be prescribed this should only be following assessment and diagnosis by a child and adolescent psychiatrist. **C**

1.6.4.3 When an antidepressant is prescribed to a child or young person with moderate to severe depression, it should be fluoxetine as this is the only antidepressant for which clinical trial evidence shows that the benefits outweigh the risks. **A**

1.6.4.4 If a child or young person is started on antidepressant medication, they (and their parent(s) or carer(s) as appropriate) should be informed about the rationale for the drug treatment, the delay in onset of effect, the time course of treatment, the possible side effects, and the need to take the medication as prescribed. Discussion of these issues should be supplemented by written information appropriate to the child or young person's and parents' or carers' needs that covers the issues described above and includes the latest patient information advice from the relevant regulatory authority. **GPP**

1.6.4.5 A child or young person prescribed an antidepressant should be closely monitored for the appearance of suicidal behaviour, self-harm or hostility, particularly at the beginning of treatment, by the prescribing doctor and the healthcare professional delivering the psychological therapy. Unless it is felt that medication needs to be started immediately, symptoms that might be subsequently interpreted as side effects should be monitored for 7 days before prescribing. Once medication is started the patient and their parent(s) or carer(s) should be informed that if there is any sign of new

symptoms of these kinds, urgent contact should be made with the prescribing doctor. **GPP**

1.6.4.6 When fluoxetine is prescribed for a child or young person with depression, the starting dose should be 10 mg daily. This can be increased to 20 mg daily after 1 week if clinically necessary, although lower doses should be considered in children of lower body weight. There is little evidence regarding the effectiveness of doses higher than 20 mg daily. However, higher doses may be considered in older children of higher body weight and/or when, in severe illness, an early clinical response is considered a priority. **GPP**

1.6.4.7 When an antidepressant is prescribed in the treatment of a child or young person with depression, and a self-report rating scale is used as an adjunct to clinical judgement, this should be a recognised scale such as the Mood and Feelings Questionnaire (MFQ). **GPP**

1.6.4.8 When a child or young person responds to treatment with fluoxetine, medication should be continued for at least 6 months after remission (defined as no symptoms and full functioning for at least 8 weeks); in other words, for 6 months after this 8-week period. **C**

1.6.4.9 If treatment with fluoxetine is unsuccessful or is not tolerated because of side effects, consideration should be given to the use of another antidepressant. In this case sertraline or citalopram are the recommended second-line treatments.[6] **B**

1.6.4.10 Sertraline or citalopram should only be used when the following criteria have been met. **C**

- The child or young person and their parent(s) or carer(s) have been fully involved in discussions about the likely benefits and risks of the new treatment and have been provided with appropriate written information.

[6] Sertraline and citalopram do not have a UK Marketing Authorisation for use in depression in children and adolescents under the age of 18 years at the date of publication (September 2005); check the Summary of Product Characteristics for current licensed indications; see also page 10.

This information should cover the rationale for the drug treatment, the delay in onset of effect, the time course of treatment, the possible side effects, and the need to take the medication as prescribed; it should also include the latest patient information advice from the relevant regulatory authority.

- The child or young person‘s depression is sufficiently severe and/or causing sufficiently serious symptoms (such as weight loss or suicidal behaviour) to justify a trial of another antidepressant.
- There is clear evidence that there has been a fair trial of the combination of fluoxetine and a psychological therapy (in other words that all efforts have been made to ensure adherence to the recommended treatment regimen).
- There has been a reassessment of the likely causes of the depression and of treatment resistance (for example other diagnoses such as bipolar disorder or substance abuse).
- There has been advice from a senior child and adolescent psychiatrist – usually a consultant.
- The child or young person and/or someone with parental responsibility for the child or young person (or the young person alone, if over 16 or deemed competent) has signed an appropriate and valid consent form.

1.6.4.11 When a child or young person responds to treatment with citalopram or sertraline, medication should be continued for at least 6 months after remission (defined as no symptoms and full functioning for at least 8 weeks). **C**

1.6.4.12 When an antidepressant other than fluoxetine is prescribed for a child or young person with depression, the starting dose should be half the daily starting dose for adults. This can be gradually increased to the daily dose for adults over the next 2 to 4 weeks if clinically necessary, although lower doses should be considered in children with lower body weight. There is little evidence regarding the effectiveness of the upper daily doses for adults in children and young people, but these may be considered in older children of higher body

weight and/or when, in severe illness, an early clinical response is considered a priority. **GPP**

1.6.4.13 Paroxetine and venlafaxine should not be used for the treatment of depression in children and young people. **A**

1.6.4.14 Tricyclic antidepressants should not be used for the treatment of depression in children and young people. **C**

1.6.4.15 Where antidepressant medication is to be discontinued, the drug should be phased out over a period of 6 to 12 weeks with the exact dose being titrated against the level of discontinuation/withdrawal symptoms. **C**

1.6.4.16 As with all other medications, consideration should be given to possible drug interactions when prescribing medication for depression in children and young people. This should include possible interactions with complementary and alternative medicines as well as with alcohol and ’recreational’ drugs. **GPP**

1.6.4.17 Although there is some evidence that St John's wort may be of some benefit in adults with mild to moderate depression, this cannot be assumed for children or young people, for whom there are no trials upon which to make a clinical decision. Moreover, it has an unknown side-effect profile and is known to interact with a number of other drugs, including contraceptives. Therefore St John's wort should not be prescribed for the treatment of depression in children and young people. **C**

1.6.4.18 A child or young person with depression who is taking St John's wort as an over-the-counter preparation should be informed of the risks and advised to discontinue treatment while being monitored for recurrence of depression and assessed for alternative treatments in accordance with this guideline. **C**

1.6.5 The treatment of psychotic depression

1.6.5.1 For children and young people with psychotic depression, augmenting the current treatment plan with an atypical antipsychotic medication[7] should be considered, although the optimum dose and duration of treatment are unknown. **C**

1.6.5.2 Children and young people prescribed an atypical antipsychotic medication should be monitored carefully for side effects. **C**

1.6.6 Inpatient care

Inpatient treatment for children and young people with depression should only be considered when the patient is at significant risk of self-harm and/or needs intensive treatment or supervision not available elsewhere. The following guidance outlines the use of inpatient facilities.

1.6.6.1 Inpatient treatment should be considered for children and young people who present with a high risk of suicide, high risk of serious self-harm or high risk of self-neglect, and/or when the intensity of treatment (or supervision) needed is not available elsewhere, or when intensive assessment is indicated. **C**

1.6.6.2 When considering admission for a child or young person with depression, the benefits of inpatient treatment need to be balanced against potential detrimental effects, for example loss of family and community support. **C**

1.6.6.3 When inpatient treatment is indicated, CAMHS professionals should involve the child or young person and their parent(s) or carer(s) in the admission and treatment process whenever possible. **B**

[7] There are no atypical antipsychotic drugs with a current UK Marketing Authorisation for depression in children at the date of publication (September 2005); check the Summary of Product Characteristics of individual drugs for current licensed indications; see also page 10.

1.6.6.4 Commissioners and strategic health authorities should ensure that inpatient treatment is available within reasonable travelling distance to enable the involvement of families and maintain social links. **B**

1.6.6.5 Commissioners and strategic health authorities should ensure that inpatient services are able to admit a young person within an appropriate timescale, including immediate admission if necessary. **GPP**

1.6.6.6 Inpatient services should have a range of interventions available including medication, individual and group psychological therapies and family support. **C**

1.6.6.7 Inpatient facilities should be age appropriate and culturally enriching, with the capacity to provide appropriate educational and recreational activities. **C**

1.6.6.8 Planning for aftercare arrangements should take place before admission or as early as possible after admission and should be based on the Care Programme Approach. **GPP**

1.6.6.9 Tier 4 CAMHS professionals involved in assessing children or young people for possible inpatient admission should be specifically trained in issues of consent and capacity, the use of current mental health legislation and the use of childcare laws, as they apply to this group of patients. **GPP**

1.6.7 Electroconvulsive therapy

Electroconvulsive therapy (ECT) should be reserved for life-threatening depression unresponsive to other treatments in young people. If it is used, ECT should be used in accordance with NICE guidance (see Section 6 for details). ECT is not recommended for children (5–11 years).

1.6.7.1 ECT should only be considered for young people with very severe depression and either life-threatening symptoms (such as suicidal

behaviour) or intractable and severe symptoms that have not responded to other treatments. **C**

1.6.7.2 ECT should be used extremely rarely in young people and only after careful assessment by a practitioner experienced in its use and only in a specialist environment in accordance with NICE recommendations. **C**

1.6.7.3 ECT is not recommended in the treatment of depression in **children** (5–11 years). **C**

1.6.8 Discharge after a first episode

After full remission, children and young people who have been depressed should be followed up for a year. After discharge, those re-referred should be seen quickly and should not be placed on a routine waiting list.

1.6.8.1 When a child or young person is in remission (less than two symptoms and full functioning for at least 8 weeks) they should be reviewed regularly for 12 months by an experienced CAMHS professional. The exact frequency of contact should be agreed between the CAMHS professional and the child or young person and/or the parent(s) or carer(s) and recorded in the notes. At the end of this period, if remission is maintained, the young person can be discharged to primary care. **C**

1.6.8.2 CAMHS should keep primary care professionals up to date about progress and the need for monitoring of the child or young person in primary care. CAMHS should also inform relevant primary care professionals within 2 weeks of a patient being discharged and should provide advice about whom to contact in the event of a recurrence of depressive symptoms. **GPP**

1.6.8.3 Children and young people who have been successfully treated and discharged but then re-referred should be seen as soon as possible rather than placed on a routine waiting list. **GPP**

1.6.9 Recurrent depression and relapse prevention

Those at high risk of relapse, including those with recurrent depression, may benefit from an extended period of psychological therapy and practical help to self-monitor symptoms of relapse. They should be followed up for at least 2 years after remission, and should be seen urgently if they are re-referred.

1.6.9.1 Specific follow-up psychological therapy sessions to reduce the likelihood of, or at least detect, a recurrence of depression should be considered for children and young people who are at a high risk of relapse (for example individuals who have already experienced two prior episodes, those who have high levels of subsyndromal symptoms, or those who remain exposed to multiple-risk circumstances). **B**

1.6.9.2 CAMHS specialists should teach recognition of illness features, early warning signs, and subthreshold disorders to tier 1 professionals, children or young people with recurrent depression and their families and carer(s). Self-management techniques may help individuals to avoid and/or cope with trigger factors. **GPP**

1.6.9.3 When a child or young person with recurrent depression is in remission (less than two symptoms and full functioning for at least 8 weeks) they should be reviewed regularly for 24 months by an experienced CAMHS professional. The exact frequency of contact should be agreed between the CAMHS professional and the child or young person and/or the parent(s) or carer(s) and recorded in the notes. At the end of this period, if remission is maintained, the young person can be discharged to primary care. **C**

1.6.9.4 Children and young people with recurrent depression who have been successfully treated and discharged but then re-referred should be seen as a matter of urgency. **GPP**

1.7 Transfer to adult services

When a young person becomes 18 years of age while receiving treatment and care from CAMHS, CAMHS should continue to provide care in accordance with this guideline. CAMHS and adult services should work cooperatively using the Care Programme Approach to ensure smooth transfer to adult services for those with recurrent depression, prepare young people for transfer, and provide good information about treatment for adults, and about local services.

1.7.1 The CAMHS team currently providing treatment and care for a young person aged 17 who is recovering from a first episode of depression should normally continue to provide treatment until discharge is considered appropriate in accordance with this guideline, even when the person turns 18 years of age. **GPP**

1.7.2 The CAMHS team currently providing treatment and care for a young person aged 17–18 who either has ongoing symptoms from a first episode that are not resolving or has, or is recovering from, a second or subsequent episode of depression should normally arrange for a transfer to adult services, informed by the Care Programme Approach. **GPP**

1.7.3 A young person aged 17–18 with a history of recurrent depression who is being considered for discharge from CAMHS should be provided with comprehensive information about the treatment of depression in adults (including the NICE 'Information for the public' version for adult depression) and information about local services and support groups suitable for young adults with depression. **GPP**

1.7.4 A young person aged 17–18 who has successfully recovered from a first episode of depression and is discharged from CAMHS should not normally be referred on to adult services, unless they are considered to be at high risk of relapse (for example, if they are living in multiple-risk circumstances). **GPP**

2 Notes on the scope of the guidance

All NICE guidelines are developed in accordance with a scope document that defines what the guideline will and will not cover. The scope of this guideline was established, after a period of consultation, at the start of the guideline development process; it is available from www.nice.org.uk/page.aspx?o=87925

This guideline is relevant to children and young people from the age of 5 up to their 18th birthday inclusive with depression, their families or carers, and all healthcare professionals involved in the help, treatment and care of children and young people with depression and their families or carers. These include:

- professional groups (including general practitioners, psychiatrists, clinical psychologists, psychotherapists, mental health, community psychiatric and practice nurses, secondary care professionals, occupational therapists and physicians) who share in the treatment and care of people with a diagnosis of depression
- professionals in other health and non-health sectors who may have direct contact with, or are involved in the provision of health and other public services for, children and young people diagnosed with depression; this may include staff from schools and other educational settings, paediatric and community child health services, social services, the voluntary sector and youth offending and criminal justice teams
- those with responsibility for planning services for children and young people with depression and their families or carers – including directors of public health, NHS trust managers and managers in primary care trusts.

The guidance does not specifically address:

- depression in children 4 years of age and under and adults 18 years of age and over
- bipolar disorder
- how learning disabilities and challenging behaviour moderate the effect of various interventions

- the specific management of patients with other physical or psychiatric conditions (comorbidities).

3 Implementation in the NHS

3.1 Resource implications

Local health communities should review their existing practice in the treatment and management of depression against this guideline. The review should consider the resources required to implement the recommendations set out in Section 1, the people and processes involved, and the timeline over which full implementation is envisaged. It is in the interests of patients that the implementation timeline is as rapid as possible.

Relevant local clinical guidelines, care pathways and protocols should be reviewed in the light of this guidance and revised accordingly.

Information on the cost impact of this guideline in England is available on the NICE website and includes a template that local communities can use (www.nice.org.uk/CG028costtemplate). Detailed implementation advice and a slide set are also available on the NICE website.

3.2 General

The Healthcare Commission considers implementation of clinical guidelines to be a developmental standard. The implementation of this guideline will build on the National Service Frameworks for Children in England and Wales and should form part of the service development plans for each local health community in England and Wales.

The National Service Framework for Children is available for England from the Department of Health website (www.dh.gov.uk) and for Wales from the NHS Wales website (www.wales.nhs.uk).

3.3 Audit

Suggested audit criteria based on the key priorities for implementation are listed in Appendix D, and can be used to audit practice locally.

4 Key research recommendations

The Guideline Development Group (GDG) has made the following recommendations for research, on the basis of its review of the evidence. The Group regards these recommendations as the most important research areas to improve NICE guidance and patient care in the future.

4.1 An appropriately blinded, randomised controlled trial should be conducted to assess the efficacy (including measures of family and social functioning as well as depression) and the cost effectiveness of individual CBT, systemic family therapy and child psychodynamic psychotherapy compared with each other and treatment as usual in a broadly based sample of children and young people diagnosed with moderate to severe depression (using minimal exclusion criteria). The trial should be powered to examine the effect of treatment in children and young people separately and involve a follow-up of 12 to 18 months (but no less than 6 months).

4.2 An appropriately blinded, randomised controlled trial should be conducted to assess the efficacy (including measures of family and social functioning as well as depression) and the cost effectiveness of fluoxetine, the favoured psychological therapy (from the previous trial [4.1]), the combination of fluoxetine and psychological therapy compared with each other and placebo in a broadly based sample of children and young people diagnosed with moderate to severe depression (using minimal exclusion criteria). The trial should be powered to examine the effect of treatment in children and young people separately and involve a follow-up of 12 to 18 months (but no less than 6 months). In order for this trial to be conducted, the previous trial (4.1) needs to be completed.

Additional research

4.3 An appropriately blinded, randomised controlled trial should be conducted to assess the efficacy (including measures of family and social functioning as well as depression) and the cost effectiveness of another self-help intervention compared with computerised CBT and treatment as usual in a sample of children and young people treated in primary care who have been diagnosed with depression. The trial should be powered to examine the effect of treatment in children and young people separately and involve a follow-up of 12 to 18 months (but no less than 6 months).

4.4 A qualitative study should be conducted that examines the experiences in the care pathway of children and young people and their families (and perhaps professionals) in order to inform decisions about what the most appropriate care pathway should be.

4.5 An appropriately designed study should be conducted to compare validated screening instruments for the detection of depression in children and young people. An emphasis should be placed on examining those that use computer technology and more child-friendly methods of assessing current mood and feelings, and take into account cultural and ethnic variations in communication, family values and the place of the child or young person within the family.

5 Other versions of this guideline

The National Institute for Health and Clinical Excellence commissioned the development of this guidance from the National Collaborating Centre for Mental Health. The Centre established a Guideline Development Group, which reviewed the evidence and developed the recommendations. The members of the Guideline Development Group are listed in Appendix B. Information about the independent Guideline Review Panel is given in Appendix C.

The booklet *The guideline development process – an overview for stakeholders, the public and the NHS* has more information about the Institute's guideline development process. It is available from www.nice.org.uk/guidelinesprocess and copies can also be ordered by telephoning 0870 1555 455 (quote reference N0472).

5.1 Full guideline

The full guideline *Depression in children and young people: identification and management in primary, community and secondary care* is published by the National Collaborating Centre for Mental Health; it is available from its website (www.rcpsych.ac.uk), the NICE website (www.nice.org.uk/CG028fullguideline) and the website of the National Electronic Library for Health (www.nelh.nhs.uk).

5.2 Quick reference guide

A quick reference guide for healthcare professionals is also available from the NICE website (www.nice.org.uk/CG028quickrefguide) or from the NHS Response Line (0870 1555 455; quote reference number N0910).

5.3 Information for the public

A version of this guideline for children and young people with depression, their families or carers, and the public is available from the NICE website (www.nice.org.uk/CG028publicinfo) or from the NHS Response Line (0870 1555 455; quote reference number N0911).

6 Related NICE guidance

Eating disorders: core interventions in the treatment and management of anorexia nervosa, bulimia nervosa and related eating disorders. *NICE Clinical Guideline* No. 9 (2004). Available from www.nice.org.uk/CG009

Self-harm: the short-term physical and psychological management and secondary prevention of self-harm in primary and secondary care. *NICE Clinical Guideline* No. 16 (2004). Available from www.nice.org.uk/CG016

Anxiety: management of anxiety (panic disorder, with or without agoraphobia, and generalised anxiety disorder) in adults in primary, secondary and community care. *NICE Clinical Guideline* No. 22 (2004). Available from www.nice.org/CG022

Depression: management of depression in primary and secondary care. *NICE Clinical Guideline* No. 23 (2004). Available from www.nice.org/CG023

Post-traumatic stress disorder (PTSD): the management of PTSD in adults and children in primary and secondary care. *NICE Clinical Guideline* No. 26 (2005). Available from www.nice.org/CG026

Guidance on the use of computerised cognitive behavioural therapy for anxiety and depression. *NICE Technology Appraisal Guidance* No. 51 (2002 – note that at the time of publication NICE is reviewing this appraisal). Available from www.nice.org.uk/TA051

Guidance on the use of electroconvulsive therapy. *NICE Technology Appraisal Guidance* No. 59 (2003). Available from www.nice.org.uk/TA059

7 Review date

The process of reviewing the evidence is expected to begin 4 years after the date of issue of this guideline. Reviewing may begin earlier than this if significant evidence that affects the guideline recommendations is identified. The updated guideline will be available within 2 years of the start of the review process.

Appendix A: Grading scheme

All evidence was classified according to an accepted hierarchy of evidence that was originally adapted from the US Agency for Healthcare Policy and Research Classification (see Table 2). Recommendations were then graded A to C on the basis of the level of associated evidence or noted as a GPP (see Table 2) – this grading scheme is based on a scheme formulated by the Clinical Outcomes Group of the NHS Executive (1996).

Table 2 Hierarchy of evidence and recommendation grading scheme.

Level	Type of evidence	Grade	Evidence
I	Evidence obtained from a single randomised controlled trial or a meta-analysis of randomised controlled trials	**A**	At least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation (evidence level I) without extrapolation.
IIa	Evidence obtained from at least one well-designed controlled study without randomisation	**B**	Well-conducted clinical studies but no randomised clinical trials on the topic of recommendation (evidence levels II or III); or extrapolated from level I evidence.
IIb	Evidence obtained from at least one other well-designed quasi-experimental study		
III	Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies		
IV	Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities	**C**	Expert committee reports or opinions and/or clinical experiences of respected authorities (evidence level IV). This grading indicates that directly applicable clinical studies of good quality are absent or not readily available.
		GPP	Recommended good practice based on the clinical experience of the GDG.

Adapted from Eccles M, Mason J (2001). How to develop cost-conscious guidelines. *Health Technology Assessment* 5 (16).

NHS Executive. *Clinical Guidelines: Using Clinical Guidelines to Improve Patient Care Within the NHS*. London: 1996.

Appendix B: The Guideline Development Group

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Freud Memorial Professor of Psychoanalysis
Chief Executive, The Anna Freud Centre
Chair, Guideline Development Group

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Co-Director, The National Collaborating Centre for Mental Health
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Chief Executive Officer, The Afiya Trust
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Carer representative

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Appendix C: The Guideline Review Panel

The Guideline Review Panel is an independent panel that oversees the development of the guideline and takes responsibility for monitoring its quality. The panel includes experts on guideline methodology, healthcare professionals and people with experience of the issues affecting patients, families and carers. The members of the Guideline Review Panel were as follows.

Dr Chaand Nagpaul (Chair)

GP, Stanmore

Mr John Seddon

Patient Representative

Professor Kenneth Wilson

Professor of Psychiatry of Old Age and Honorary Consultant Psychiatrist, Cheshire and Wirral Partnership NHS Trust

Dr Paul Rowlands

Consultant Psychiatrist, Derbyshire Mental Health Services Mental Health Care Trust

Dr Roger Paxton

R&D Director, Newcastle, North Tyneside and Northumberland Mental Health NHS Trust

Appendix D: Audit criteria

Possible objectives for an audit

One or more audits could be carried out in different care settings to ensure that:

- children and young people with depression are involved in their care
- treatment options are appropriately offered and provided for children and young people with depression.

People who could be included in an audit

A single audit could include all children and young people with depression. Alternatively, individual audits could be undertaken on specific groups of individuals such as:

- a sample of children or young people from particular populations in primary care
- a sample of children or young people from particular populations in CAMHS tiers 2–4.

Measures that could be used as a basis for an audit

Please see tables on pages 51–55..

Standards	Criteria	Audit methods
Assessment and coordination of care		
When assessing a child or young person with depression, healthcare professionals should routinely consider, and record in the patient's notes, potential comorbidities, and the social, educational and family context for the patient and family members, including the quality of interpersonal relationships, both between the patient and other family members, and with their friends and peers	Clinical notes include information concerning: • life events • associated psychological factors • comorbid conditions • family context • school context • social context • family relationships • peer relationships	Case note audit of a random selection of children and young people with depression Review of service protocols for the management of depression
Treatment considerations in all settings		
Psychological therapies used in the treatment of children and young people should be provided by therapists who are also trained child and adolescent mental healthcare professionals	Services should agree minimum training criteria for healthcare professionals engaging in psychological therapy Healthcare professionals delivering psychological therapies should meet agreed minimum criteria	Review of service policies Survey of healthcare professional qualifications and CPD experience

Comorbid diagnoses and developmental, social and educational problems should be assessed and managed, either in sequence or in parallel, with the treatment for depression. Where appropriate this should be done through consultation and alliance with a wider network of education and social care	Clinical notes include information concerning: • comorbid conditions • social difficulties • educational problems Where problems in these areas are identified in case notes, evidence should exist that discussion has taken place about intervention for identified problems	Case note audit of a random selection of children and young people with depression Review of service protocols for the management of depression
Attention should be paid to the possible need for parents' own psychiatric problems (particularly depression) to be treated in parallel, if the child or young person's mental health is to improve. If such a need is identified, then a plan for obtaining such treatment should be made, bearing in mind the availability of adult mental health provision and other services	Clinical notes should record information concerning the assessment of parental mental health Where clinical notes indicate that parental mental health is of concern there should be a record of a discussion about referral to appropriate treatment services	Case note audit of a random selection of children and young people with depression
Step 1 Detection and risk profiling		
Healthcare professionals in primary care, schools and other relevant community settings should be trained to detect	Services should have training programmes for tier 1 professionals that address:	Review of service polices Review of service training records

symptoms of depression, and to assess children and young people who may be at risk of depression. Training should include the evaluation of recent and past psychosocial risk factors, such as age, gender, family discord, bullying, physical, sexual or emotional abuse, comorbid disorders, including drug and alcohol use, and a history of parental depression; the natural history of single loss events; the importance of multiple risk factors; ethnic and cultural factors; and factors known to be associated with high a risk of depression and other health problems, such as homelessness, refugee status and living in institutional settings	• detection of depressive symptoms • assessment of risk factors for depression • culturally sensitive systems for detecting and supporting children and young people with depression	Survey of tier 1 professionals' perceptions of: • availability of training • quality of training
Child and Adolescent Mental Health Services (CAMHS) tier 2 or 3 should work with health and social care professionals in primary care, schools and other relevant community settings to provide training and develop ethnically and culturally sensitive systems for detecting, assessing, supporting and referring children and young people who are either depressed or at significant risk of becoming depressed	See above	See above
Step 2 Recognition		

Training opportunities should be made available to improve the accuracy of CAMHS professionals in diagnosing depressive conditions. The existing interviewer-based instruments (such as Kiddie-Sads [K-SADS] and Child and Adolescent Psychiatric Assessment [CAPA]) could be used for this purpose but will require modification for regular use in busy routine CAMHS settings	Services should have training programmes for CAMHS professionals across all tiers that address the detection and diagnosis of depression in children and young people	Review of service polices Review of service training records Survey of CAMHS professionals' perceptions of: • availability of training • quality of training Review of teaching methods used
Step 3 Mild depression		
Antidepressant medication should not be used for the initial treatment of children and young people with mild depression	Children and young people presenting with mild depression should not be prescribed antidepressant medication as a first-line intervention	Children and young people prescribed antidepressants in primary care, child health or CAMHS could be identified using pharmacy records. Those identified could be surveyed to establish that other psychological therapies had been offered before the antidepressant was prescribed
Steps 4 and 5 Moderate or severe depression		
Children and young people with moderate to severe depression should be offered, as a first-line treatment, a specific psychological therapy (individual cognitive behavioural therapy [CBT], interpersonal therapy or	Psychological therapies should be offered before medication Psychological therapies should be:	Review of service protocols for treatment of depression Review of service protocols for delivering psychological therapies

shorter-term family therapy; it is suggested that this should be of at least 3 months' duration)	• time limited • structured • cognitive behavioural therapy, family therapy or interpersonal therapy	Structured review of case notes of a random representative sample of children and young people with depression
Antidepressant medication should not be offered to a child or young person with moderate to severe depression except in combination with a concurrent psychological therapy. Specific arrangements must be made for careful monitoring of adverse drug reactions, as well as for reviewing mental state and general progress; for example, weekly contact with the child or young person and their parent(s) or carer(s) for the first 4 weeks of treatment. The precise frequency will need to be decided on an individual basis, and recorded in the notes. In the event that psychological therapies are declined, medication may still be given, but as the young person will not be reviewed at psychological therapy sessions, the prescribing doctor should closely monitor the child or young person's progress on a regular basis and focus particularly on emergent adverse drug reactions	Children or young people on antidepressant medication should have been offered psychological therapy Where children and young people have been offered medication, systems must be in place for regular monitoring of side effects. Where children and young people are not receiving psychological therapy, regular meetings must be held (at least monthly in the first 3 months of treatment) to monitor side effects Children and young people and their parent(s) or carer(s) must have been informed of the risks as well as benefits of antidepressant medication	Structured review of case notes of a random representative sample of children and young people with depression Survey of patients and families/carers to establish whether information about risks and side effects has been provided

Appendix E: Assessing the severity of depression in primary care

Key symptoms

At least one of the following symptoms are present on most days, most of the time, for at least 2 weeks:

- Persistent sadness or low (irritable)[8] mood
- Loss of interests and/or pleasure
- Fatigue or low energy.

If any key symptoms are present, ask about associated symptoms

- Poor or increased sleep
- Poor concentration or indecisiveness
- Low self-confidence
- Poor or increased appetite
- Suicidal thoughts or acts
- Agitation or slowing of movements
- Guilt or self-blame.

[8] Whilst this is a well-documented feature it is not currently listed in ICD-10 diagnostic criteria.

Then ask about past history of depression, family history, associated disability and availability of social support

1. **Factors that favour <u>general advice and watchful waiting</u>**
    - Four or fewer of the above symptoms
    - No past or family history
    - Social support available
    - Symptoms intermittent, or of less than 2 weeks' duration
    - Patient is not actively suicidal
    - Little associated disability.

2. Factors that favour <u>more active treatment in primary care</u>

- Five or more symptoms
- Past history or family history of depression
- Low level of social support
- Suicidal thoughts
- Associated social disability.

3. Factors that favour <u>referral to mental health professionals</u>

- Poor or incomplete response to two interventions
- Recurrent episode within 1 year of previous one
- Patient or relatives request referral
- Self-neglect.

4. Factors that favour <u>urgent referral to a psychiatrist</u>

- Actively suicidal ideas or plans
- Psychotic symptoms
- Severe agitation accompanying severe (seven or more) symptoms
- Severe self-neglect.

ICD-10 definitions
Mild depression: four symptoms
Moderate depression: five or six symptoms
Severe depression: seven or more symptoms, with or without psychotic features

Appendix F: Glossary

Active listening A way of listening that focuses entirely on what the other person is saying and confirms understanding of both the content of the message and the emotions and feelings underlying the message to ensure that understanding is accurate.

Adherence The behaviour of taking medicine according to treatment dosage and schedule as intended by the prescriber. In this guideline, the term adherence is used in preference to the term compliance, but is not synonymous with concordance, which has a number of different uses and meanings.

Adverse drug reaction Any undesirable experience that results from the administration of a pharmacologically active agent.

Bipolar disorder This condition is also known as manic depression. It is an illness that affects mood, causing a person to switch between feeling very low (depression) and very high (mania).

CAMHS Child and Adolescent Mental Health Service(s).

CAMHS link worker See **Primary mental health worker**

Care Programme Approach (CPA) Introduced in 1991, this approach was designed to ensure that different community services are coordinated and work together towards a particular person's care. This approach requires that professionals from the health authority and local authority get together to arrange care, and applies to all patients accepted for care by the specialist mental health services.

Child An individual aged 5–11 years.

Child and Adolescent Psychiatric Assessment (CAPA) An interviewer-based diagnostic interview with versions for use with children and their parent(s).

Cognitive behavioural therapy (CBT) A range of behavioural and cognitive behavioural therapies, in part derived from the cognitive behavioural model of affective disorders, in which the patient works collaboratively with a therapist using a shared formulation to achieve specific treatment goals. These may include recognising the impact of behavioural and/or thinking patterns on feeling states and encouraging alternative cognitive and/or behavioural coping skills to reduce the severity of target symptoms and problems.

Conversational technique This term is used in the guideline to emphasise the importance of a two-way communication. A collaboration between patient and healthcare professional aims to ensure that the patient feels able to express their feelings in the healthcare setting safe in the knowledge that their healthcare professional will listen.

Depression (major depressive disorder) The guideline uses the ICD-10 definition in which ‘an individual usually suffers from depressed mood, loss of interest and enjoyment, and reduced energy leading to increased fatiguability and diminished activity. Marked tiredness after only slight effort is common. Other symptoms are: (a) reduced concentration and attention; (b) reduced self-esteem and self-confidence; (c) ideas of guilt and unworthiness (even in a mild type of episode); (d) bleak and pessimistic views of the future; (e) ideas or acts of self-harm or suicide; (f) disturbed sleep; (g) diminished appetite.‘

Depression unresponsive to treatment Depression that has failed to respond to two or more antidepressants taken at an adequate dose for an adequate duration given sequentially.

Dysphoria An emotional state characterised by malaise, anxiety, depression or unease.

Dysthymia A chronic depression of mood which does not currently fulfil the criteria for recurrent depressive disorder, of mild or moderate severity, in terms of either severity or duration of individual episodes. There are variable phases of mild depression and comparative normality. Despite tiredness, feeling down and not enjoying much, people with dysthymia are usually able to cope with everyday life.

Effectiveness The extent to which a specific intervention, when used under ordinary circumstances, does what it is intended to do. Clinical trials that assess effectiveness are sometimes called management trials.

Efficacy The extent to which an intervention produces a beneficial result under ideal conditions. Clinical trials that assess efficacy are sometimes called explanatory trials and are restricted to participants who fully cooperate. The randomised controlled trial is the accepted 'gold standard' for evaluating the efficacy of an intervention.

Electroconvulsive therapy (ECT) A therapeutic procedure in which an electric current is briefly applied to the brain to produce a seizure. This is used for treatment of severe depression symptoms or to ease depression that isn't responding well to other forms of treatment. It is sometimes called convulsive therapy, electroshock therapy or shock therapy.

Family therapy Family therapy sessions based on systemic, cognitive behavioural or psychoanalytic principles, which may include psychoeducational, problem-solving and crisis management work, and might involve specific interventions with a depressed child or young person.

Guided self-help A self-administered intervention designed to treat depression, which makes use of a range of books or a self-help manual that is based on an evidence-based intervention and is designed specifically for the purpose.

Guideline Development Group (GDG) The group of academic experts, clinicians and service user representatives responsible for developing the guideline.

Guideline implementation Any intervention designed to support the implementation of guideline recommendations.

Guideline recommendation A systematically developed statement that is derived from the best available research evidence, using predetermined and

systematic methods to identify and evaluate evidence relating to the specific condition in question.

Healthcare professionals A generic term used in this guideline to cover all health professionals such as GPs, psychologists, psychotherapists, psychiatrists, paediatricians, school doctors, nurses (including school and community based), health visitors, counsellors, art therapists, music therapists, drama therapists and family therapists who work with children and young people and whose work may involve considering the young person's additional psychological needs.

Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS) An interviewer-led procedure for diagnostic assessment of depression including the severity of the current episode designed for use by trained individuals with some clinical experience with participants aged 6–17 years.

Meta-analysis The use of statistical techniques in a systematic review to integrate the results of several independent studies.

Mild depression Four depressive symptoms as defined by the ICD-10.

Moderate depression Five or six depressive symptoms as defined by the ICD-10.

Mood and Feelings Questionnaire (MFQ) A self-report measure used to screen for depression.

Multidisciplinary review A comprehensive review of the child or young person's situation that involves professionals additional to the therapist(s) delivering treatment. This review should consider a range of sources of information including evidence of functioning at home, school and other relevant settings and should take account of the wishes of the child or young person and their parent(s) or carer(s).

Multidisciplinary team For the purposes of this guideline this term refers to professionals who are involved in the care of a child or young person working in partnership across all tiers. Members of the team are likely to include

healthcare professionals (including CAMHS professionals, GPs, health visitors and school nurses), teachers, social services and voluntary agencies.

Non-directive supportive therapy (NDST) This therapy involves the planned delivery of direct individual contact time with an empathic, concerned and skilled non-specialist CAMHS professional to offer emotional support and non-directive problem solving as appropriate and to review the child or young person's state (for example, depressive symptoms, school attendance, suicidality, recent social activities) in order to assess whether specialist help is needed.

Primary mental health worker (PMHW) Sometimes also called 'CAMHS link worker'. This role was described in *NHS Health Advisory Service, Together We Stand* (London: NHS Health Advisory Service, 1995) and was recommended as a way of improving the relationship, communication and collaboration between specialist mental health services (CAMHS) and the wider network of services working with children, such as schools, youth and community services, primary care, etc. Primary mental health workers tend to operate in tiers 1 and 2. In some parts of the UK, including Scotland, this has led to the establishment of PMHW posts. In other areas the role has been developed, but delivered in a variety of ways. In some cases, workers are employed specifically to deliver primary mental health work, whilst in others, this work is achieved though an extension of pre-existing professional roles.

Psychoanalytic/psychodynamic child psychotherapy Psychodynamic interventions are defined as psychological therapies derived from a psychodynamic/psychoanalytic model, and where:

1. Therapist and patient explore and gain insight into conflicts and problem behaviours, modes of thought and relating and how these are represented in current situations and relationships including the therapy relationship (for example, transference and counter-transference).

2. This leads to patients being given an opportunity to explore through play, drawing, talking and behaviour, feelings and conscious and unconscious conflicts, originating in the past or in learnt behaviour. The

technical focus is on interpreting and working through conflicts and recurrent problematic areas of behaviour and relating as they manifest in the treatment situation.

3. Therapy is non-directive and recipients are not taught specific skills (such as thought monitoring, re-evaluating, or problem solving).

Psychological therapies A group of treatment methods that involve psychosocial rather than physical intervention. They include cognitive behavioural therapy, family therapy, systemic family therapy, non-directive supportive therapy, psychodynamic psychotherapy, group psychotherapy, counselling, art therapy, interpersonal psychotherapy, guided self-help and any other form of treatment that aims to be helpful through the communication of thoughts and feelings in the presence of a therapist, who works with the material using a systematic framework for understanding and responding to it.

Racial identity status An individual's perception of himself or herself as belonging to a racial group; also the beliefs, morals and attitudes that are shared with a particular racial group in contrast with other groups. It has been suggested that racial identity is integral to personality and is a key dynamic factor in psychotherapeutic dyads.

Randomisation A method used to generate a random allocation sequence, such as using tables of random numbers or computer-generated random sequences. The method of randomisation should be distinguished from concealment of allocation, because if the latter is inadequate, selection bias may occur despite the use of randomisation. For instance, a list of random numbers may be used to randomise participants, but if the list were open to the individuals responsible for recruiting and allocating participants, those individuals could influence the allocation process, either knowingly or unknowingly.

Randomised controlled trial (RCT) (also termed **randomised clinical trial**) An experiment in which investigators randomly allocate eligible people into groups to receive or not to receive one or more interventions that are being compared. The results are assessed by comparing outcomes in the different

groups. Through randomisation, the groups should be similar in all aspects apart from the treatment they receive during the study.

Recurrent depression The development of a depressive disorder in a person who has previously suffered from depression.

Relapse The reappearance of disease signs and symptoms after apparent remission. The definitions of relapse used in the review in the guideline were those adopted by the individual studies and varied between studies.

Remission Diminution or disappearance of symptoms.

Risk profiling A structured assessment and analysis of those factors in a child or young person's environment and history that are known to increase the risk of depression.

Screening Screening is defined by the Guideline Development Group as a simple test performed on a large number of people to identify those who have depression.

Self-help Any activity or lifestyle choice that an individual makes in the belief that it will confer therapeutic benefit.

Severe depression Seven or more depressive symptoms as defined by the ICD-10.

Sleep hygiene Behavioural practices that promote continuous and effective sleep.

Stepped care A considered, organised, coordinated approach to screening, assessment, treatment and onward referral by an individual practitioner, team or care provider organisation, within the parameters of defined protocols or pathways. These approaches may or may not be provided within the context of a fixed budget (for example, the Health Maintenance Organisation [HMO] in the USA). Primary care trusts are required to develop protocols for the treatment of depression in primary care within the National Service Framework for Mental Health.

Stepped-care model A sequence of treatment options offering simpler and less expensive interventions first and more complex and expensive interventions if the patient has not benefited, based on locally agreed protocols.

Subsyndromal depression (subthreshold depression) Depressive symptoms that fail to meet the criteria for major depressive disorder. This type of depression is not covered by this guideline.

Suicidal ideation Thoughts about suicide or of taking action to end one's own life.

Tier 1 Primary care services including GPs, paediatricians, health visitors, school nurses, social workers, teachers, juvenile justice workers, voluntary agencies and social services.

Tier 2 CAMHS Services provided by professionals relating to workers in primary care including clinical child psychologists, paediatricians with specialist training in mental health, educational psychologists, child and adolescent psychiatrists, child and adolescent psychotherapists, counsellors, community nurses/nurse specialists and family therapists.

Tier 3 CAMHS Specialised services for more severe, complex or persistent disorders including child and adolescent psychiatrists, clinical child psychologists, nurses (community or inpatient), child and adolescent psychotherapists, occupational therapists, speech and language therapists, art, music and drama therapists, and family therapists.

Tier 4 CAMHS Tertiary-level services such as day units, highly specialised outpatient teams and inpatient units.

Tricyclic antidepressants (TCAs) The original class of antidepressants used to treat depression by increasing levels of the neurotransmitters serotonin and noradrenaline.

Watchful waiting An intervention in which no active treatment is offered to the person with depression if, in the opinion of the healthcare professional, the

person may recover without a specific intervention. All such patients should be offered a follow-up appointment.

Young person An individual between the age of 12 and their 18th birthday.

F32 Depressive episode

In typical mild, moderate, or severe depressive episodes, the patient suffers from lowering of mood, reduction of energy, and decrease in activity. Capacity for enjoyment, interest, and concentration is reduced, and marked tiredness after even minimum effort is common. Sleep is usually disturbed and appetite diminished. Self-esteem and self-confidence are almost always reduced and, even in the mild form, some ideas of guilt or worthlessness are often present. The lowered mood varies little from day to day, is unresponsive to circumstances and may be accompanied by so-called "somatic" symptoms, such as loss of interest and pleasurable feelings, waking in the morning several hours before the usual time, depression worst in the morning, marked psychomotor retardation, agitation, loss of appetite, weight loss, and loss of libido. Depending upon the number and severity of the symptoms, a depressive episode may be specified as mild, moderate or severe.

Incl.: single episodes of:
- depressive reaction
- psychogenic depression
- reactive depression

Excl.: adjustment disorder (F43.2)
recurrent depressive disorder (F33.-)
when associated with conduct disorders in F91.- (F92.0)

F32.0 Mild depressive episode

Two or three of the above symptoms are usually present. The patient is usually distressed by these but will probably be able to continue with most activities.

F32.1 Moderate depressive episode

Four or more of the above symptoms are usually present and the patient is likely to have great difficulty in continuing with ordinary activities.

F32.2 Severe depressive episode without psychotic symptoms

An episode of depression in which several of the above symptoms are marked and distressing, typically loss of self-esteem and ideas of worthlessness or guilt. Suicidal thoughts and acts are common and a number of "somatic" symptoms are usually present.

Agitated depression Major depression Vital depression	single episode without psychotic symptoms

F32.3 Severe depressive episode with psychotic symptoms

An episode of depression as described in F32.2, but with the presence of hallucinations, delusions, psychomotor retardation, or stupor so severe that ordinary social activities are impossible; there may be danger to life from suicide, dehydration, or starvation. The hallucinations and delusions may or may not be mood-congruent.

Single episodes of:
- major depression with psychotic symptoms
- psychogenic depressive psychosis
- psychotic depression
- reactive depressive psychosis

F32.8 Other depressive episodes

Atypical depression
Single episodes of "masked" depression NOS

F32.9 Depressive episode, unspecified

Depression NOS
Depressive disorder NOS